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BRITISH MEDICAL JOURNAL

LONDON SATURDAY SEPTEMBER 10 1949

CENTENARY OF PAVLOV'S BIRTH

BY

E. D. ADRIAN, O.M., M.D., F.R.C.P., F.R.S.

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Ivan Petrovich Pavlov was born a hundred years ago in Ryazan, a district town in Central Russia. He died in 1936, one of the great men of his time, of immense prestige in his own country and famous throughout the world for his scientific achievements. We are too close to him to forecast the verdict of future generations, or rather to know which phase of his work will seem the most important, but we are fortunately not too far off to remember what he was like. Many of us have witnessed the energy, the sincerity, and the buoyant enthusiasm which made him such a universal favourite. He was a great character—outspoken, impatient, and fiery-tempered, with an engaging simplicity and delight in work and play.

To the physiologist, Pavlov's work covers several fields and goes back almost to the beginning of the modern era, to the time of Ludwig and Heidenhain. To the world at large it has come to be identified with the single bold conception of the conditioned reflex. The idea that intelligent behaviour might be reduced to such a basis was welcomed by some as a new and inspiring philosophy and dismissed by others as wicked nonsense. It was seldom viewed as the working hypothesis for a new kind of experiment. It was like Pavlov to take such a novel and simple generalization as the basis for his work on the brain, but in the end the generalization may have less importance than the facts it produced. And even if Pavlov had never worked on the brain he would still have been one of the outstanding physiologists of his age. He had won the Nobel prize for his researches on digestion at a time when his conditioned reflex experiments had scarcely begun.

An excellent account of Pavlov's career has been given by his old pupil, Professor Anrep (1936). He was the eldest son of a parish priest and was a vigorous child, delighting in all forms of physical achievement. An accident postponed his schooling and he was not particularly distinguished as a scholar, but in 1870 he entered the Faculty of Science of the University of St. Petersburg and came under the influence of Cyon, who was then professor of physiology. Cyon, the discoverer of the cardiac depressor nerve, suggested a problem on the innervation of the pancreas, and Pavlov did so well in his first research that he was awarded the gold medal of the University.

Experimental Work

In 1875 Cyon was elected as professor at the Medical Academy and took Pavlov as his assistant, but the election was revoked by the Government. Pavlov indignantly refused to serve under Cyon's successor and moved to the Veterinary Institute. In 1879 he became medically qualified, and a few years later he completed his training by working in Germany with the two leaders of experimental physiology—Ludwig, the exponent of precise method in the study of the circulation, and Heidenhain, the investigator of secretory processes. Under their influence, on his return to Russia he settled down to work first on the innervation of the heart and then on the secretion of the digestive glands.

He was already an experimental surgeon of great dexterity, and he had come to realize that in the study of normal digestion the well-being of the animal was essential. Discomfort and anaesthesia were both eliminated, and his dogs were trained to co-operate fully in the experiment. The result was a revolution in the technique of investigating the digestive tract. There were the sham feeding method, the innervated Pavlov pouch, and the Eck fistula, and all his work revealed a direct grasp of essentials and a mastery of experimental detail. He discovered the secretory nerves of the stomach and pancreas, the acid control of the pyloric sphincter, the nervous and chemical phases of gastric secretion, and the action of enterokinase. In fact, most of our present knowledge of the physiology of digestion is based on the work done in Pavlov's laboratory between 1888 and 1906. In 1904 he was awarded the Nobel prize for this work, and in 1907 was elected a Foreign Member of the Royal Society.

It is sometimes said that the discovery of secretin by Bayliss and Starling in 1902 made Pavlov realize that future work on the digestive system would lie with the physiological chemist. But his decision to turn from the study of digestion to that of brain function was probably inevitable. The nervous control of digestion always interested him far more than the chemical, and he had already discovered a kind of nervous control which cried out for further investigation. The secretion of saliva was produced reflexly by food in the mouth or by the smell of food, but it was also produced by the sight of food—i.e., by a visual pattern customarily associated with feeding. Pavlov called this the psychic secretion. He soon found that the stimulus need not be visual; the sound of the dinner bell could be made just as evocative as the sight of the dinner. In fact, the dog could be trained so that it would salivate to a particular stimulus or combination of stimuli which had no necessary connexion with food. The reaction had the almost mechanical certainty of the reflex, but it depended on the higher levels of the nervous system. Although expressed by the secretion of a digestive gland, it seemed to be on a par with other kinds of behaviour involving learning, recognition, and intelligence.

Conditioned Reflexes

From 1905 onwards Pavlov settled down to investigate these conditioned reflexes, and for the rest of his life he was constantly at work on them. We do not yet know what neural processes take place in the brain when a new habit is formed, but what we do know about animal and human behaviour has been enormously extended by what Pavlov found out. He used a new method of experiment and a new way of treating the results. Thorndyke had studied the associative processes in animals by experiments in which the solution of a simple problem was rewarded by food. His results were published in 1898 in his book, *The Animal Intelligence*, which is now one of the classics of experimental psychology. Pavlov studied the formation of reactions associated with feeding, but he deliberately excluded the subject-matter of psychology. He believed that the physiologist ought to keep to his proper sphere, that nothing but confusion would come if he began to speak or think of learning, of fears and hopes, success or failure. He must confine himself to an objective analysis of the external stimuli and of the animal's behaviour. He must "adhere strictly to the physiological point of view, investigating and systematizing the whole subject by physiological methods alone." This is easier said than done: the exclusion of the familiar terms which we use to describe our own behaviour often seems to involve a complex restatement in which half the picture is left out. But Pavlov adhered strictly to his principle, and was justified by the discoveries which it brought. He set himself to study not "learning" but the "formation of conditioned reflexes," and he succeeded in demonstrating many of the rules which govern their formation.

Pavlov has been praised or blamed because his thesis could be taken to mean that men are machines and should be treated as such. Naturally he wanted to see how widely his physiological net could be cast, and he was human enough, one might almost say naughty enough, to enjoy the reaction of his hearers when he discussed religion as an example of the social conditioned reflexes. But his real concern was with the experiments he was making to cover the borderline between innate and acquired reactions. The value of his way of approach is shown not only by what he himself found out but by the whole development of behaviour studies in the past thirty years.

There is no doubt at all about the value of the method. The conditioned reflex is now used as one of the standard tools for investigating the capacity of the nervous system. It can be used to study the range of sensory discrimination, the effects of cerebral injury, etc., for Pavlov has shown how conditioned reflexes can be formed and kept in being, and for many purposes that is enough. We need not try to understand the underlying changes which must have taken place in the nervous system.

A Good Working Hypothesis

There is naturally more doubt about the detailed scheme which Pavlov elaborated to account for his findings. It invoked a number of special processes assumed to take place in the brain—irradiation, positive and negative induction, extinction, inhibition, and generalization. It became more elaborate as the work progressed. The cortex was thought of as a mosaic of excitatory and inhibitory points with further excitatory and inhibitory influences spreading out by irradiation or concentrated in particular regions. The scheme is difficult to follow, partly because some of the terms carry unfamiliar meanings and partly because Pavlov was constantly adding to it. It had to reconcile a vast number of experimental results, and we may be sure that it was never wholly satisfactory to its originator. But for Pavlov it certainly fulfilled the function of a good working hypothesis in that it was continually leading to fresh investigations; it was a spur to his original genius, but was not without danger to the many pupils who were dominated by his thought. Like so many biological theories it became a dogma not to be challenged except in inessentials, and so prevented the fusion of the brain physiology of Pavlov's school with that studied in other countries by different methods and from a different starting-point.

There were, of course, many other reasons to prevent a complete interchange of ideas, and it is a mistake to suppose that Pavlov's views have been immune from criticism in his own country. His genius would have dominated less ardent minds wherever he had happened to work; in the U.S.S.R. Beritoff has been an outspoken critic for many years, and Anokhin and Kupalov have both upheld objections on specific points. Fortunately a monograph has now been published by Konorski (1948), an old pupil of Pavlov's, which will help to remove the misconceptions which have grown up. It is a criticism of Pavlov's scheme and an attempt to bring his work into line with recent neurophysiological research, but it also gives an impressive picture of the range and exactitude of the experiments of his school and of the hard thinking which went to their interpretation. Konorski finds Pavlov's scheme inadequate because the original conceptions were never clearly defined and so could be used, and often were used, to mean different things. He says, "For as long as the great edifice of knowledge built up by Pavlov was guided and extended under that great scientific genius it could continue to grow despite its isolation and despite the fundamental inadequacy of its construction"; but he feels that "Pavlov's priceless heritage" will be lost if there is no synthesis with other lines of advance in the physiology of the nervous system.

"Use Facts and Do Not Theorize"

It is doubtful whether a complete synthesis can be made without first pulling down much of the edifice which has been built up so carefully, but this does not mean that the work was wasted. Anrep tells us that theoretical interpretations in general had little value for Pavlov: "Use facts and do not theorize," was his constant saying. He has given us a host of facts relating to the plasticity of the brain, and the facts were selected to reveal the general principles of habit formation, not to vindicate a particular theory of cortical activity.

Pavlov worked on conditioned reflexes for the last 30 years of his life. He had neither the time nor the temperament required for the lengthy experimental work; indeed, Anrep records that Pavlov never attempted to establish a conditioned reflex himself, but he was in close touch with the many experiments going on under his direction. The work was constantly expanding into newer and larger institutes, yet he was able to manage them and to direct a host of research workers without losing contact with their problems. He could do this because he had immense reserves of physical energy and was able to switch his mind completely and without effort to the task before him. He could be the scientist, the administrator, the family man, the gardener, the book collector, or the naturalist. He could fill each role with enthusiasm. He could be a charming host or guest in spite of language barriers.

Many physiologists will remember the impressive sincerity of his presidential address to the International Physiological

Congress in Leningrad in 1935. He warned us that the ties of international science would not be strong enough to prevent war, though war is "essentially a bestial method of settling difficulties, a method unworthy of the human mind with its unlimited resources." But the Congress promised new friendships and was altogether a splendid affair, a fitting tribute to its world-renowned president. He was in his 86th year, a venerable but not an aged figure. He died six months later, after a short illness.

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MYXOEDEMATOUS MADNESS

BY

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Myxoedema is one of the most important, one of the least known, and one of the most frequently missed causes of organic psychoses—important because it may respond so gratifyingly to treatment, little known because little has been written about it, often missed because the textbook description of myxoedema is not the rule but the exception.

Fourteen cases are here described, all of which had myxoedema and psychotic changes. In every one of them the diagnosis was confirmed beyond doubt. They all showed a psychosis amounting to complete "madness," ten being admitted to the mental observation wards under the Lunacy Act, one referred to the neurosurgeon for cerebral tumour, and three to general medical wards with other diagnoses. In nine of the cases there was a dramatic and complete recovery of sanity with thyroid treatment, in two there was partial improvement, one showed no change, and two patients died. The fact that in none of these cases had the diagnosis been made by the outside doctor suggests that there is need for increased awareness of myxoedema as a cause of psychoses, and, further, shows that it may be worth while discussing how myxoedema can be diagnosed so that cases may be recognized and treated early.

The average doctor is well aware that dullness and a poor memory are caused by myxoedema, but does not realize that a frank psychosis can occur. Dr. Leonard Simpson, in Price's *Medicine*, describes the condition clearly and stresses its importance, but most of the popular textbooks omit any reference to it at all, and this may account for the rarity of its recognition. Apart from medical textbooks, A. J. Cronin (1937) paints a vivid if sensational picture of a "mad myxoedema," and it was from this source that I first learned of the condition. Though Stoll (1932) described six personal cases, the fact that Zondek and Wolfsohn (1944) published one solitary case of myxoedematous psychosis in 1944 suggests again that it is regarded as a rarity. Nevertheless, the condition was clearly described, and was recognized as exceedingly common by the Committee of the Clinical Society of London (1888) appointed in 1883 to consider the subject of myxoedema. Their report says (p. 31): "Delusions and hallucinations occur in nearly half the cases, mainly where the disease is advanced. Insanity as a complication is noted in about the same proportion as delusions and hallucinations. It takes the form of acute or chronic manias, dementia, or melancholia, with a marked predominance of suspicion and self-accusation." (At the time of that report thyroid treatment was quite unknown, so doubtless many of the cases would to-day have been diagnosed and treated before mental symptoms arose.) I want to make it clear that I am not describing something new, but something old that is nowadays often forgotten.

Is there a Specific Type of Psychosis Associated with Myxoedema?

This question is fully discussed by Akelaitis (1936). The possible theories are: (1) that myxoedema produces a psychosis depending on the "pre-psychotic reaction type"; (2) that it produces a specific type of psychosis; and (3) that it produces psychoses of various types, either resembling one of the ordinary idiopathic psychoses or else typical of no special type.

Cases in the literature record a very wide variety of mental changes, and certainly in the series I have observed there has been no constant type of psychosis, though general confusion and disorientation with persecutory delusions and hallucinations, and occasional bouts of restless violence, have been common. I have made the diagnosis on the myxoedematous appearance of the patient and not on the kind of mental symptoms. No physician would attempt to diagnose lobar pneumonia or typhoid by the delirium they may produce, and likewise in myxoedema it is the disease which is the characteristic feature, not its mental manifestations.

The fact that recorded cases of myxoedema psychosis have closely resembled paranoia (Case 1 and Stoll, 1932), schizophrenia (Zondek and Wolfsohn, 1944), melancholia (Buschan, 1896), or other orthodox psychoses does suggest that the common psychoses—schizophrenia, mania, melancholia, paranoia, and so on—may turn out to be not diagnoses in themselves, but manifestations of underlying organic disease.

Does the Response to Thyroid Prove the Myxoedematous Origin of the Psychosis?

First, if the case responds it is of course no absolute proof, because almost any type of psychosis can improve spontaneously. Nevertheless, when mental symptoms that have been present in a hypothyroid patient for many months clear dramatically within a few weeks of starting thyroid it is reasonably certain that they were due to myxoedema.

Secondly, if the mental changes persist after adequate thyroid treatment, does this mean they were not myxoedematous? As Ruhberg (1936) points out: "It is necessary to determine if they are secondary to thyroid insufficiency or merely a coincident concomitant." He states dogmatically: "If the mental symptoms are part of myxoedema, improvement and relief should be obtained by establishing a normal basal metabolic rate." Akelaitis (1936), discussing cases which showed physical but not mental improvement with thyroid, also concludes: "The psychosis was a coincidence and not part of the myxoedema." Such dogmatic assumptions are unjustified. It is generally agreed that metabolic changes can produce irreversible damage—for instance, the changes of prolonged hypoglycaemia or of pellagra may fail to respond respectively to glucose or to the vitamin B complex, although they were caused by deprivations of these. Again, the belated treatment of cretinism shows that the changes in the brain cannot be reversed by thyroid.

Dr. Leonard Simpson (personal communication) records such a case in which peculiar behaviour persisted after thyroid treatment and ultimately ended in psychosis. Hence

prolonged thyroid deficiency may well cause a psychotic change which does not respond to thyroid. I believe that myxoedema, if left untreated, can produce an incurable psychosis, and I consider that those cases that have not been completely cured (Cases 1, 2, and 8) with thyroid were nevertheless initially caused by lack of thyroid, especially as two of them improved a great deal at the beginning of treatment.

I can give no certain evidence (from analysing these fourteen cases) that the longer the myxoedema is left untreated the poorer is the outlook for recovery, though this is what one would expect. It is so hard to determine when the myxoedema started that one can only guess at the answer.

Case 1

A housewife aged 55 was admitted on an authorized officer's order on Aug. 26, 1944, confused, hallucinated, and with persecutory ideas. Fourteen years previously she took her child to another hospital with a whitlow. The casualty officer, noticing that she herself looked thyrotoxic, referred her to a surgeon. Total thyroidectomy was performed. On discharge she was instructed to take thyroid, but stopped doing so after five years. She had thus been without thyroid for the nine years preceding her admission. For three years her daughters had noticed her increasing deafness, hoarseness of voice, and mental strangeness. She believed neighbours and others were plotting to harm her; she heard imaginary voices, and sometimes expressed delusions of grandeur.

On examination she was seen to be mentally retarded, apathetic, and sluggish. Occasionally she would become excited and complain of hearing voices or that the nursing staff was plotting to kill her. She was so confused and disorientated that she was unable to give an account of herself. She had the typical appearance of advanced myxoedema with gross non-pitting oedema of the whole body. She had well-marked supraclavicular pads, scanty eyebrows, thick croaking voice, and dry scaly skin. She was slow and ponderous in both body and mind. Her pulse was 65 and the blood cholesterol 362 mg. per 100 ml.; it was not possible to take the basal metabolic rate.

In addition to myxoedema she had gross elephantiasis of the left leg with scars of a previous Kondoleon operation. This elephantiasis had come on rapidly eight years previously. At the time of the operation (four years previously at another hospital) the house-surgeon, after describing the leg, records: "whole body now solid with lymphatic oedema." This suggests that she was really grossly myxoedematous at that time, but that because she had lymphatic oedema of the leg the generalized swelling was incorrectly assumed to be lymphatic oedema also.

Progress.—She was treated with 1 gr. (65 mg.) of thyroid four times daily, increasing by 1 gr. a day till she was taking 8 gr. (0.52 g.) daily. The blood cholesterol came down as follows: Aug. 29, 362 mg. per 100 ml.; Sept. 5, 354 mg.; Sept. 18, 230 mg.; Sept. 26, 158 mg. The thyroid was then reduced to 1 gr. four times daily, whereupon the cholesterol rose to 273 mg. by Oct. 13. The thyroid was again increased to 2 gr. (0.13 g.) four times daily and the cholesterol came down again; thus on Oct. 24 it was 225 mg. and on Nov. 7 163 mg. It therefore seemed that she required this large dose of 8 gr. a day, and, having had a *total* thyroidectomy, this was not surprising. During treatment her physical improvement was slow and her mental improvement disappointing. After six weeks she had lost 7 lb. (3.18 kg.) in weight and her appearance was noticeably less myxoedematous. Mentally there was an increase in alertness and sufficient decrease in disorientation and noisiness for her to be transferred from the mental observation ward to a general medical ward on Oct. 19; but she continued (though less constantly) to behave peculiarly and she had to be sent back to the observation ward on Nov. 6. Three months after admission (Nov. 28) she had lost over 14 lb. (6.35 kg.) in weight and the improvement in her appearance was more apparent, but as she did not show any further mental improvement she was transferred to Shenley Mental Hospital. Though she still thought other patients were making accusations against her and stated that she and King George VI jointly owned the hospital, there was a great improvement compared with her mental state on admission, for she could give a full account of her previous history and was far less confused.

Case 2

A housewife aged 60 was admitted on an authorized officer's order on Dec. 20, 1945, with delusions of persecution and hallucinations. For six months she had noticed that her voice was croaking and she felt cold weather badly, but she had noted no other myxoedematous symptoms—no gain in weight, falling out of hair, or deafness. During the week before admission she had an idea that her landlord was trying to poison her "because she knew all about the shootings in the back garden," she heard voices talking to her continuously, and locked herself in her room to protect herself from imaginary enemies.

On examination she was completely confused and disorientated, and showed the delusions and hallucinations described above. Her appearance was that of advanced myxoedema, with puffy face, malar flush, toad-like skin, scanty hair, and croaking nasal voice. She slept a great deal, with unusually sonorous snoring. The pulse was 60, cholesterol 374 mg. per 100 ml., basal metabolic rate −26%, blood pressure 170/90.

Progress.—She was treated with 1 gr. of thyroid thrice daily, starting on Dec. 24. She made steady improvement, both mental and physical: after a week she lost her delusions and realized that they had been absurd. After a fortnight she was rational, orientated, and almost completely clear. After three weeks she had lost 14 lb. (6.35 kg.) in weight and now slept without snoring. (This was a particularly striking feature of the case.) Her appearance was much improved and the blood cholesterol had come down from 374 to 250 mg. per 100 ml. After a month she was transferred to a general medical ward for a cataract operation. She stayed there five months because her eye was slow to clear up and there was delay over her new glasses. She behaved rationally most of the time, but occasionally complained that she was being watched. She was discharged for convalescence on June 7, 1946.

Two months later she wrote to the ward sister complaining that she was under the control of a mysterious man's voice, and on Sept. 7, three months after her discharge, she was readmitted to the mental observation wards complaining that this man's voice was talking to her all the time and controlling her actions. On readmission her blood cholesterol was 276 mg. per 100 ml. and her basal metabolic rate was −25%. She did not look frankly myxoedematous. Treatment with 2 gr. (0.13 g.) of thyroid thrice daily brought her blood cholesterol down to 150 mg. in three weeks, but there was no corresponding mental improvement, and on Nov. 15 she was certified and transferred to Shenley Mental Hospital.

Case 3

A housewife aged 50 was admitted on an authorized officer's order on Aug. 16, 1946, with delusions and hallucinations. For three months she had been getting increasingly dull mentally, gaining weight, and becoming constipated. For one week she had expressed ideas of persecution, saying that many people were plotting against her. She also believed that she was ridden with incurable diseases, and that she might infect everyone. She was continuously terrified by strange voices and strange faces.

On examination she was hallucinated, deluded, and persecuted as described above. She told the doctor estimating her basal metabolic rate that he was in danger of catching typhoid, syphilis, and cancer if he came near her. She was slow in her responses and very depressed and disorientated. Her appearance was typically myxoedematous. The "strawberry and cream" complexion was well marked (the malar flush shows

FIG. 1.—Case 3; Aug. 26, 1946.

FIG. 2.—Case 3; April 14, 1947.

well in Fig. 1, which also shows that the outer thirds of the eyebrows *can* be well developed in myxoedema) and the palpebral tissues were narrowed by compression with myxoedematous tissue. The voice was thick, grating, and nasal. Her hair was coarse but profuse, and her skin thick and scaly. The pulse was 76, cholesterol 428 mg. per 100 ml., basal metabolic rate −25%, and blood pressure 155/110.

Progress.—On Aug. 23 she was given 1 gr. of thyroid twice daily, the dose being gradually increased to 2 gr. three times a day on Sept. 12. There was a very rapid improvement in both her appearance and her mental state. Unfortunately, the first photograph (Fig. 1) was taken when she had received thyroid for three days, and shows a perceptibly less myxoedematous state than on admission. Within 10 days she was much more alert, and as well as being free from delusions and hallucinations she had insight—realizing the foolishness and absurdity of her previous ideas. Her cholesterol had come down from 428 to 253 mg. per 100 ml., but her basal metabolic rate was still −22%. When she had become clear-minded she told us that she had been in Redhill Hospital two years before, where she had been given some tablets which made her feel brighter and thinner. (Inquiries at Redhill disclosed that she had been an in-patient there from Nov. 12 to 21, 1944, suffering from myxoedema, and had rapidly improved with 2 gr. of thyroid thrice daily. After discharge her practitioner had discontinued the treatment.) Her mental and physical improvement continued rapidly; she was discharged to the out-patient department a month after admission and continues to attend there in very good health. Fig. 2 shows her appearance on April 14, 1947.

Case 4

A housewife aged 73 was admitted on Dec. 23, 1946, as a case of "bronchitis." On admission she was quite confused, could give no coherent history at all, and was obviously grossly demented. She showed no evidence of actual delusions or hallucinations. A history was not available.

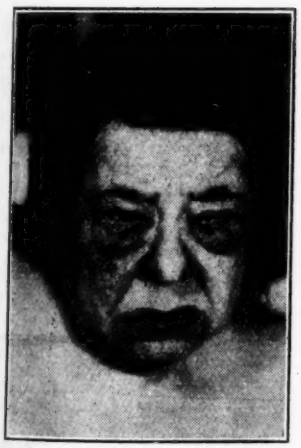

FIG. 3.—Case 4. This patient collapsed suddenly six days after admission.

On examination she was stuporous and slow, had occasional bouts of restlessness, and was grossly demented. She was flagrantly myxoedematous (Fig. 3). Her whole body was spongy with myxomatous tissue, which was especially striking around the eyes and above the clavicles, and which distended the lower lip. Her voice was thick, croaking, and nasal in character. She breathed with a thick, stertorous snorting sound. Her hair was scanty. Her colouring was of the classical pink-and-white variety. The pulse was 60 and the cholesterol 166 mg. per 100 ml. (a surprisingly low figure). She was too ill for the basal metabolic rate to be taken. The blood pressure was not recordable.

Progress.—She was given thyroid, ¼ gr. (32 mg.) thrice daily, on admission, increased two days later to 1 gr. thrice daily. Five days after admission she became more restless and confused, disturbing the rest of the ward. The next day she suddenly collapsed, became cyanosed and unconscious, with bubbling respiration, and died shortly afterwards.

Post-mortem examination showed a small thyroid (13 g.) with normal macroscopic appearance, but microscopically showing marked fibrosis, atrophy of the lobules, and almost complete absence of colloid, with replacement by lymphoid tissue. The heart (480 g.) showed myocardial hypertrophy of both ventricles, with gross dilatation of the right heart. The lungs showed congestion and oedema, with some pus in the trachea and main bronchi.

Case 5

A housewife aged 72 was admitted to a medical ward on Jan. 6, 1947, having collapsed unconscious five hours before admission. She was just recovering consciousness when admitted. For two years she had been putting on weight and feeling tired, drowsy, and unusually cold. She had also noticed her hair falling out and her hearing getting worse. On the day of admission she collapsed unconscious, with snoring respiration,

FIG. 4.—Case 5; Jan. 6, 1947.

FIG. 5.—Case 5; Jan. 1, 1948.

On admission she was slow and inclined to ramble, though rational and orientated. Two days later she became completely confused, noisy, and irrational. She had no idea where she was, and repeatedly said, "I must go home and look after my son." The other patients were so much upset by her restless mutterings that she had to be transferred to the mental observation ward.

She had a typical myxoedematous appearance and colouring. The oedema of her eyelids was particularly pronounced; her left eye, blind and atrophied after an old injury, was completely occluded by myxomatous swelling, and appeared visible only after thyroid treatment. The pulse was 70, cholesterol 320 mg. per 100 ml., blood pressure 220/120. The basal metabolic rate could not be taken.

Progress.—She was started on thyroid, ¼ gr. (16 mg.) twice daily on Jan. 7, increased gradually to 2 gr. three times a day on Jan. 18. There was rapid improvement in both her mental confusion and her myxoedematous appearance (see Figs. 4 and 5). (Note how the atrophied left eye, previously walled in by oedema, has become visible as the swelling subsided.) The blood cholesterol came down from 320 to 130 mg. in a fortnight. She became mentally quite clear within a week and was transferred back to a general medical ward. After a month she was discharged perfectly clear mentally, and physically free from any signs of myxoedema. She continues to attend the out-patient department for further supplies of thyroid.

Case 6

A woman of no occupation aged 67 was admitted on an authorized officer's order on Feb. 4, 1947, demented, confused, and disorientated. Her landlady said that for three years she had been "going senile." She needed reminding about everything and took two hours to get ready to go out. Once a fine pianist, she had lost all interest in music. During the week before admission she had attacks of screaming and violence, set her nightgown on fire, and became generally quite unmanageable.

On examination she was so slow and lethargic that she would fall asleep while being interviewed; she was quite confused and out of touch with the world, and was unable to give any account of herself whatever.

Physically, she gave an immediate impression of myxoedema. She had the pink-and-white complexion; coarse, thick skin and hair; slow, deep, nasally obstructed voice; and scanty eyebrows. The pulse was 66, cholesterol 300 mg. per 100 ml., blood pressure 156/100. The basal metabolic rate could not be taken.

Progress.—On Feb. 4 she was started on ¼ gr. of thyroid three times a day, gradually increasing to 2 gr. three times a day on Feb. 24. There was a rapid improvement in both her appearance and her sanity. Within a fortnight she was fit for a general ward and within a month was discharged. Her blood cholesterol had fallen from 300 mg. per 100 ml. on admission to 125 mg. on discharge. She attends her own doctor for further supplies of thyroid, and is in good physical and mental health.

Case 7

A housewife aged 54 was admitted on an authorized officer's order on March 13, 1947, with alternating excitement and depression, and ideas of persecution. For one year she had been getting slow and dull, and losing interest in herself and the house. A marked increase in weight and coarsening of her features had been noticed by her relatives. Her sister-in-law said: "When I was in a hospital once I saw somebody with 'lack of thyroid,' and she looked just like my sister-in-law does now, so I've always thought she must have the same illness. I tried to persuade her to see a doctor, but she wouldn't go." For a week before admission she had been alternately excitable and depressed, at times behaving violently. She had told her relatives that various people were plotting to do her harm and she had accused her husband of attempting to poison her.

On examination she was depressed, confused, and persecuted. She babbled disconnected nonsense about fire-and-water vengeance and the Bible, and could not give any rational account of herself. Whenever anyone approached her bed she would cling to their hands, begging for mercy. She showed the appearance of advanced myxoedema (Fig. 6). Her face was bloated and she had a butterfly-shaped flush on the nose and

FIG. 6.—Case 7; March 13, 1947.

FIG. 7.—Case 7; April 21, 1947.

FIG. 8.—Case 7; April 6, 1949.

cheeks. Her skin was thick and rough. Her voice was thick and hoarse, with a nasally obstructed quality. The lips were noticeably thickened. The scalp hair was fine and plentiful, the eyebrows sparse. The pulse was 60, blood cholesterol 364 mg. per 100 ml., blood pressure 180/110. The basal metabolic rate was impossible to take.

Progress.—On March 14 she was given thyroid, ½ gr. three times a day, increased gradually to 2 gr. three times a day on March 20. At first there was rapid improvement in her physical appearance, with no corresponding mental change. Fig. 7 shows clearly both the depressed mental state and the striking change in facial appearance after a month's treatment. Her blood cholesterol came down from 364 to 226 mg. in three weeks. Her depression, persecutory ideas, and general unruliness continued for five weeks, and, if anything, thyroid treatment seemed to lend more vigour to her misbehaviour—she was a sore trial to everyone. Then suddenly on April 21 she became rational, cheerful, and orientated, with almost complete amnesia over her period of confusion. For a further week she had occasional bouts of weeping, after which time she remained cheerful, happy, and perfectly normal both mentally and physically (Fig. 8). She continues to attend as an out-patient, in vigorous health.

Case 8

A housewife aged 62 was admitted on an authorized officer's order on May 15, 1947, with systematized delusions. Her sister said she had always been rather simple. For one month she had become restless and deluded. She wandered round the house, packing up her belongings and saying that she was going to the seaside. She maintained solidly that she and her husband had a house at Leigh-on-Sea, and that there she must go (there was no truth in this whatever).

FIG. 9.—Case 8; May 18, 1947.

FIG. 10.—Case 8; July 4, 1947.

On examination she was quiet and co-operative, but incapable of giving a history and unwilling to submit to a basal-metabolic-rate test. She insisted that her husband was living somewhere in the hospital. Throughout her stay she persisted with the delusion that she had a house at Leigh-on-Sea. She was a shrivelled little old lady, not very myxoedematous to look at (see Fig. 9). She had wrinkled dry skin of yellowish parchment colour. There was gross alopecia. Her voice was high, with a grating, scrannel character, but was not the usual myxoedematous voice. There were no other signs. The pulse was 80 and the blood cholesterol 400 mg. per 100 ml.; the basal metabolic rate was impossible to obtain, and the blood pressure was not taken.

Progress.—She was started on thyroid, 1 gr. thrice daily, gradually increasing to 3 gr. thrice daily. There was a steady change in her appearance, as can be seen from Fig. 10. Within six weeks she looked 15 years younger. The blood cholesterol came down steadily thus: May 15, 400 mg. per 100 ml.; May 25, 349 mg.; June 4, 287 mg.; June 24, 218 mg. It was most disappointing that there was no corresponding mental improvement. She persisted in her delusions with, if anything, more conviction and vigour than before. I waited two months to see if the psychosis would clear, and then, on July 9, transferred her to Shenley Mental Hospital as a certified patient.

Case 9

A housewife aged 56 was transferred from Hillingdon Hospital on May 28, 1947, for investigation as a case of suspected cerebral tumour or subdural haematoma. She had already been diagnosed as suffering from myxoedema.

One year previously she had been admitted to Hillingdon as a possible case of Alzheimer's disease. At that time she complained of six months' chronic head pains, depression, loss of concentration, and attacks of palpitations and panic. She was said to have been a lively person and good company before the illness, but had become so dull she could not work out ordinary money problems. On that admission nothing abnormal was noted, though she was observed to have an unusually deep, husky voice. She was discharged slightly improved after three weeks.

She was readmitted to Hillingdon on April 26, 1947, suffering from right thoracic herpes zoster and mental symptoms. She was completely confused, and was comatose most of the time but occasionally restless and violent.

Physical examination revealed an appearance of myxoedema. She had a sallow thick skin, a husky deep voice, and scanty eyebrows. There were oedematous pads above both clavicles and she was very deaf. The pulse was 90, basal metabolic rate −27%, blood cholesterol 333 mg. per 100 ml., blood pressure 200/120.

She was treated with thyroid, 3 gr. daily for 14 days, reduced after three weeks to 1 gr. daily. During a bout of restlessness on May 4 she fell out of bed and sustained a large haematoma in the centre of the forehead. Because of increased mental confusion and a suggestion of early papilloedema she was transferred on May 28 to the Central Middlesex County Hospital under Mr. T. I. G. James for neurosurgical investigation.

On admission she was still mildly myxoedematous in appearance. The blood cholesterol was 272 mg. per 100 ml., the pulse 75. No abnormal neurological findings were made. The encephalogram was normal. It was therefore considered that her mental symptoms were myxoedematous. The dose of thyroid was increased to 2 gr. three times a day. She was transferred back to Hillingdon on June 16, where, with further thyroid treatment, her mental condition gradually became normal and she was discharged for convalescence on July 11.

Case 10

A housewife aged 64 was admitted to Hillingdon Hospital under Dr. C. G. Barnes on Feb. 21, 1948, as a case of "chronic heart and renal back pressure." Dr. Barnes kindly asked me to see her on Feb. 27. Her husband stated that for one year her face had been getting puffy, for six months she had swelling of the legs and difficulty in walking, and for one month she had been bedridden. A week before admission she became quite confused and delirious, and remained so until the day of admission, when she became comatose.

On examination she was semicomatose, with shallow respiration and a slow pulse. Her eyes were completely closed by oedema and could not be opened. Her face was typical of an unusually advanced degree of myxoedema, with a striking yellow skin and malar flush. She was partially bald, her eyebrows were scanty, and her eyelashes almost completely absent. The pulse was 60 and blood cholesterol 486 mg. per 100 ml.; the basal metabolic rate was impossible to obtain.

She was given 10 gr. (0.65 g.) of thyroid the same day, as Dr. Barnes feared that otherwise she would suffocate or die from bronchopneumonia.

Progress.—During the next two days she became more deeply comatose, but on the third day she became conscious and her eyes were visible. She was restless and hallucinated. She complained that "Joe the Shadow" was trying to do her harm and that people were watching her. She shouted about pictures on the ceiling and told me that she heard pianos and singing. She remained maniacal and hallucinated for over a fortnight. She was given 1 gr. of thyroid daily and her myxoedematous appearance and her mental state steadily improved. After two months she looked nearly normal and her confusion had almost gone. On April 1 the basal metabolic rate was +2% and the blood cholesterol had come down from 486 to 314 mg. per 100 ml. She was discharged home on April 1, fit and rational.

Case 11

A housewife aged 53 was admitted on Feb. 23, 1948, complaining of tiredness and undue gain in weight. Fifteen months previously she had had a cholecystectomy for gall-stones. For six months she had felt weary and had gained much weight. She complained of chronic catarrh and said her voice had become coarse and her skin rough.

On examination she was slow and rather drowsy, but appeared rational until a week later, when she showed delusions of persecution. She said she had been accused of wrongdoing by the hospital staff and believed that she had been admitted for punishment. She told me that all the other patients were whispering to each other, saying unpleasant things about her. She had to be transferred to the mental observation ward on March 8, as her paranoid ideas were getting worse.

Physically she had the typical appearance of fully developed myxoedema. Her features were swollen, the normal facial creases being ironed out by the swelling. Her face was a waxy yellow colour. Her eyebrows were scanty, her skin dry, her speech thick and indicative of nasal obstruction. Her

FIG. 11.—Case 11; Feb. 24, 1948.

FIG. 12.—Case 11; June 14, 1948.

blood cholesterol was higher than that of other cases in this series—610 mg. per 100 ml. The palms of her hands had yellow bands 0.25 cm. wide, corresponding to the creases. These were cholesterol deposits, the same colour as the xanthelasma of hypercholesterolaemia, and they steadily faded during the next two months as the blood cholesterol fell with treatment. (The high blood cholesterol might also have contributed to the gall-stones from which she had suffered.) The pulse was 75 and the basal metabolic rate −8%; the blood pressure was 155/90.

Progress.—She was given thyroid, 1 gr. three times a day, on Feb. 27, increasing gradually to 2 gr. four times daily on March 19. At first her mental symptoms grew worse, while her appearance improved. By March 11 she had some insight into her previous irrationality, and by March 13 she was mentally normal, remaining so until her discharge to the outpatient department on March 25. Figs. 11 and 12 show the striking changes in her face.

Case 12

This patient was a physician aged 33. During a lecture on myxoedema to some doctors taking a membership course in 1946 I described the mental changes which I had so often encountered, and mentioned that ideas of persecution were common. At the end of the lecture the patient came up to me and explained that he was a known case of myxoedema, and gave the following history.

In 1941, while with the Army in West Africa, he felt tired, dull, and slow. At the same time he developed ideas of persecution. These symptoms continued unchanged until February, 1942, when he was diagnosed as a definite case of myxoedema and ordered thyroid, 3 gr. daily. The persecutional ideas disappeared completely in a short time and he felt a

striking improvement in his feeling of well-being. In 1945, while in Italy, he began to wonder if it was really necessary to go on taking thyroid, so he stopped. The mental symptoms crept insidiously back and there was a falling off in his general efficiency. Eventually he found himself unwilling to go into the mess with his fellow officers because he believed they were talking about him, criticizing him, and plotting against him in some way. He resumed thyroid treatment again, and his persecutional ideas once more disappeared rapidly. Since that time he has continued to take thyroid in various doses, at present being stabilized on 6 gr. daily and remaining mentally and physically quite well.

When I saw him his appearance seemed normal (I did not examine him professionally), but he had some malar flush and his voice was a little lower and slower than the average. He had not previously mentioned his mental symptoms to anyone lest they indicated a true psychotic tendency, but on learning that they were merely a part of his hypothyroid symptoms he was much relieved and quite pleased to admit them. He has very kindly agreed to my publishing these details about his case.

Case 13

A housewife aged 62 was admitted on March 18, 1949, on an authorized officer's order, suffering from confusion and dementia. Her husband said that for about four years she had been increasingly slow in mind and body. She often complained of coldness and deafness, and became very forgetful. She "snored something awful." A week before admission she became unable to walk. Her voice was so thick no one could understand her. She stared blankly about her and seemed unaware of what was going on.

On examination she was mentally in a state of hibernation, and an unintelligible croaking monosyllable was the only reply to questioning. Her mind seemed to have stopped functioning rather than to have become disordered.

Physically she was the grossest case of myxoedema in the series. Her face was bloated and misshapen, with great wine-coloured patches on a dusky yellow background. She was dirty, unkempt, and partially bald. Her skin was as cold and rough as a lizard's. Her pulse was 48, temperature 97° F. (36.1° C.), respirations 16.

FIG. 13.—Case 13. This patient died on the day after admission.

Progress.—She died early the next morning before any investigations had been done, so the cholesterol value, the basal metabolic rate, and the blood pressure were not known. A coroner's inquest reported death from acute heart failure due to myxoedema. The thyroid was completely replaced by white fibrous tissue, but was otherwise normal in size and shape. The heart was dilated and hypertrophied, and there was a pericardial effusion.

Case 14

A housewife aged 53 was admitted on an authorized officer's order on March 29, 1949, suffering from hallucinations and delusions of persecution. For three months she had complained that she was being persecuted by the people in the flat above her. She tried to persuade her husband that they were spying upon her down a ventilator pipe. She heard voices saying unpleasant things to her, particularly at night. She also began to snore excessively, and because of this she went to the out-patient E.N.T. department of a large voluntary hospital. Her delusions and hallucinations were so flagrant, however, that she was immediately referred to the psychiatric department. The senior psychiatrist then referred her to the authorizing officer as a case of paranoid psychosis.

When deliberately questioned she admitted that for two years her hair had been coming out, her voice had been getting deeper, and her skin had become dry. She said she felt so cold and sleepy she wanted to curl up and go into a long, long sleep.

On examination she was found to be persecuted, deluded, and hallucinated, and she complained of the voices pestering her continually. She was typically though not grossly myxoedematous. The skin of her face was yellow with a malar flush, the palpebral fissures were narrow, and the eyebrows scanty. Her voice was thick and croaking. Her pulse was 68, cholesterol 250 mg. per 100 ml., blood pressure 130/90. The basal metabolic rate was impossible to take (she thought she was being gassed).

FIG. 14.—Case 14; March 31, 1949.

FIG. 15.—Case 14; May 25, 1949.

Progress.—She was started on thyroid, ½ gr. thrice daily, increased five days later to 1 gr. thrice daily. Within a fortnight there was an obvious facial change and she began to have insight into her hallucinations—admitting they were not real voices though she still heard them. After three weeks the cholesterol had come down from 250 to 120 mg., the hallucinations had stopped, and she said, "I feel different, I see things different, and my husband says I look younger. I talk different; I've lost that deep tone and seem to speak lighter." She was discharged a month after admission and continues to attend as an out-patient in normal physical and mental health. Soon after discharge, when she went to her grocer he said to her: "Are you a relation of the Mrs. — who used to come in here and went to hospital?" He had completely failed to recognize her.

Discussion

It is hoped that publication of these fourteen case reports may call attention to the very important fact that myxoedema causes psychosis. If one observer can encounter this number in four years it must mean that there are many others. Possibly there are many cases in mental hospitals which have not been diagnosed. If the diagnosis is borne in mind by psychiatrists a number of otherwise hopeless psychoses may be cured, and the awareness of an organic cause for one psychosis may lead to the discovery of physical causes for others which are at present dismissed as of psychological or idiopathic origin.

How to Diagnose Myxoedema

As this paper has stressed the importance of early diagnosis and treatment of myxoedema, it seems logical to summarize the methods by which a diagnosis can be made, especially as these case records show that in no instance was the diagnosis made before the patient came to hospital.

The history gives little help in making a diagnosis, though it greatly helps in confirming it once the condition is suspected. That is because the symptoms are admitted rather than complained of; they are dismissed by the patient as minor nuisances rather than exhibited as major complaints, and are therefore usually elicited only when the appropriate questions are asked. The mental slowness of the illness itself smothers self-criticism, and so changes may pass unnoticed by the patient while friends and relations observe them. In fact, you get no history of myxoedema if you are not thinking of myxoedema when you take that history.

The following symptoms are common: general tiredness, gain in weight, vague aching pains in the legs, poor memory, constipation, deafness, falling out of hair, dry skin, always feeling cold. All these symptoms commonly occur in non-myxoedematous people and not one of them is constant in myxoedema. Change in the facial appearance, alteration in the voice, and snoring are usually noticed by relatives rather than by the patient.

The only way to ascertain what a case of myxoedema looks like is to see one. No amount of description can convey the unmistakable impression of a well-developed case. Photographs are more helpful than words, but give no idea of the characteristic colouring and voice. Here is a description of an advanced case.

Nearly all cases occur in women. The features look bloated and the normal contours of the face are smoothed away, just as the wrinkles of a balloon disappear when it is blown out. Oedema collects in the lips, broadening them, and around the eyes, forming little bags of flesh beneath them. When, after treatment, the swelling round the eyes subsides there is sometimes revealed a slight exophthalmos, possibly due to the anterior pituitary's efforts to flog an inactive thyroid. The colour is yellowish and waxy, with a contrasting burgundy-coloured flush over the malar bones. The hair is dry and scanty, the receding hair margin leaves a wide forehead, and there may be partial baldness. The eyebrows are sparse, and sometimes the lashes too. The classical loss of hair over the outer third of the eyebrows is an unreliable sign, because so many normal people show this deficiency.

The voice is slow and fumbling from the clumsy thickness of the lips and tongue, and the oedematous infiltration of the nasal passages gives it a characteristic nasal quality. It is impossible to imprison the sound in words, but the impression is that of a bad gramophone record of a drowsy, slightly intoxicated person with a bad cold and a plum in the mouth. Snoring (Morehead, 1936), already mentioned as a symptom, may be of arresting intensity, and it is odd that in a discussion on snoring at the Royal Society of Medicine no mention was made of myxoedema as one of its causes.

The description here given is that of an unusually obvious case. The recognition of an early or a mild case is harder but is more satisfying than recognizing the self-evident one. Mild cases are probably often missed because the textbook illustrations always picture an unusually gross case and not the moderate cases which are more often encountered. Mistakes are also made through expecting every sign to be present, whereas the average case lacks at least one of the classical features of the illness; for example, Case 3 had luxuriant eyebrows (see Fig. 1), Case 4 had a low blood cholesterol, Case 8 had no puffiness of the face (see Fig. 9), Case 9 had a raised pulse, and Case 11 had a normal basal metabolic rate.

Confirmatory Tests

Photographic Test.—I consider there is only one infallible confirmatory test for myxoedema. Take a good photograph; then give thyroid for a month or more and take another photograph. The change between the two photographs is a clear confirmation of the diagnosis. In many cases where I have not been certain of the diagnosis the change recorded by photographs has been the only unequivocal proof of the answer. Look at the picture of Case 8 (Fig. 9), which might well be that of just an elderly bald lady: the change of face makes the diagnosis certain, especially coupled with the changes in cholesterol. See also Cases A and B—two other examples of "non-obvious" myxoedema confirmed by photographic changes (Figs. 16, 17, 18, 19, and 20). These cases are not included in the series, because they had no psychosis: and here I would like to stress that only a proportion of myxoedema cases have psychotic changes, and that these remarks on the diagnosis of myxoedema apply to all cases, with or without mental symptoms.

FIG. 16.—Case A; May 20, 1947.

FIG. 17.—Case A; July 2, 1947.

FIG. 18.—Case A; Nov. 19, 1947.

FIG. 19.—Case B; Jan. 13, 1948.

FIG. 20.—Case B; May 10, 1948.

Blood Cholesterol.—This is nearly always raised, and, furthermore, descends with thyroid treatment. In ten of these cases the initial blood cholesterol was 300 mg. or more per 100 ml., and it usually descended by over 100 mg. per 100 ml. after thyroid treatment. Blood cholesterol estimations are, after photographs, the best confirmatory tests.

Basal Metabolic Rate.—From experience with many other cases besides these I have found the basal metabolic rate of little help in diagnosing myxoedema. It is a test which is accepted when it agrees with the physician and disregarded when it does not. I have seen many cases of myxoedema with normal or raised B.M.R. Further, the presence of mental change or respiratory obstruction may prevent the estimation being done. In only four of the cases described above was the basal metabolic rate taken—Case 2 −26%, Case 3 −25%, Case 9 −27%, Case 11 −8%.

Pulse Rate.—The classical bradycardia of the textbook is not common. In four cases the pulse was over 70 and in only two instances was it below 60.

Blood Pressure.—In six of these cases there was hypertension (either a systolic pressure above 170 mm. Hg or a diastolic pressure above 100 mm. Hg).

Summary

Myxoedema is a much commoner cause of psychosis than is usually believed. Treatment with thyroid usually cures the psychosis dramatically. Fourteen cases are described—nine recovered completely, two recovered partially, one showed no change, and two were fatal. There is no specific psychosis, but paranoid ideas are common. A description of myxoedema is given and methods of diagnosing it are reviewed. Photographs before and after thyroid treatment give the best confirmation of the diagnosis.

I want to thank the visiting doctors and magistrates who left cases uncertified so that I could keep them for thyroid treatment rather than transfer them to a mental hospital. Also I must thank Miss Buckle and Mr. Booker for their excellent photographs. I am indebted to Dr. Barnes, of Hillingdon, for Case 10, to Mr. Iltydd James for Case 9, and to Dr. Pagel for the necropsy on Case 4. Dr. Leonard Simpson has given advice and criticism.

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OPTIMAL METHODS IN THE TREATMENT OF OPHTHALMIA NEONATORUM

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The relative value of sulphanilamide, sulphapyridine, sulphamezathine, sulphathiazole, and sulphadiazine in the treatment of ophthalmia neonatorum has been discussed in a previous study (Sorsby, 1945). It was pointed out that, with the dose of 0.25 g. on admission and 0.125 g. four-hourly day and night until 48 hours after clinical cure, the results obtained by different sulphonamides were essentially the same, and that sulphanilamide itself and sulphapyridine were less desirable than sulphamezathine and sulphathiazole and sulphadiazine, as they tended to give toxic symptoms rather more frequently.

Sulphamezathine seemed to be at least as satisfactory as sulphathiazole and sulphadiazine, but, like the other drugs, still gave a residue of about 15% of cases that responded either poorly or showed relapse. In a series of 84 cases treated with sulphamezathine a clinical cure was obtained within one to three days in 39.3%, 44% required four to eight days' treatment, whilst 16.7% showed an unsatisfactory response or a relapse.

The different modes of using penicillin were found to give a high rate of adequate results only when penicillin locally was applied in high concentration and at frequent intervals (Sorsby, 1947). In a series of 104 cases treated initially at intervals of one minute for half an hour (with drops in a concentration of 2,500 units per ml. in 71 cases, and a concentration of 10,000 units per ml. in 33 cases) the average total time of treatment was 38 hours. This, however, applied to only 77 of the 104 cases, while 27 showed a poor response or relapse. Likewise there were six unsatisfactory results in a total of 39 cases treated by systemic injections (800,000 units: four injections of 200,000 units each at four-hourly intervals).

Taking the whole series of 333 cases treated with sulphonamides and 143 cases treated intensively with penicillin, the percentage of failures—assessed by poor response or relapse—was considerable in both series: 16.3% with sulphonamides and 23.1% with penicillin. It was pointed out, however, that unsatisfactory response is to be understood in a relative sense only. In not a single instance was the response so poor as to cause anxiety for the state of the eye, and some of the cases classified as relapses were almost certainly cases of reinfection rather than relapse. The present study, covering 151 cases, was undertaken to determine whether better results could be obtained, particularly from the sulphonamides, by more intensive use of the agents employed.

A Series of 151 Cases

Table I sets out the 151 cases studied, classified according to causal organism and severity of the affection in relation to mode of treatment. It will be seen that *Staphylococcus albus* was responsible for the largest number of cases (33), *Staphylococcus aureus* for 22, various bacilli, including diphtheroids, for 21, and the gonococcus for 14 cases. There were 31 cases completely negative, showing neither organism nor inclusion bodies, whilst 18 cases showed no organisms but had inclusion bodies. In addition, inclusion bodies were seen in combination with causal organisms in 25 cases. The total incidence of inclusion bodies in this series was therefore 43. Of the whole series 48 cases were mild, 78 moderate, and 25 severe. The different grades of severity seemed to be fairly evenly distributed over the whole range of causal organisms. Several modes of treatment were tried out in this series.

Therapeutic Results

1. *Systemic Penicillin Therapy (30 Cases).*—In all 30 cases were treated by penicillin systemically. Four received 800,000 units of penicillin exclusively by mouth—200,000 units initially with a second dose one and a half to three hours later, and two further doses at three-hourly intervals. The response was slow and incomplete, and all four cases relapsed. This method was not tried further. Twenty-six cases received an initial intramuscular injection of 200,000 units, followed by the same dose orally one and a half to three hours later, and subsequently by two further doses by mouth at three-hourly intervals. All the 26 cases recovered, but 11 relapsed. As the method was obviously inferior to treatment by four intramuscular injections it was discontinued.

2. *Treatment by Oral Sulphamezathine with an Initial Dose of 0.5 g. and a Maintenance Dose of 0.25 g. at Six-hourly Intervals (57 Cases).*—In the previously reported series of 84 cases treated by sulphamezathine the initial dose was half that in the present series and the maintenance dose also half, but given at four-hourly instead of six-hourly intervals. The total dose of sulphamezathine was therefore increased on the first day from 0.875 g. to 1.25 g., and on subsequent days from 0.75 g. to 1 g. Table II sets out the comparative results in the two series. It will be seen

TABLE I.—*Classification of Cases by Causal Organism and Severity in Relation to Mode of Treatment*

	Penicillin Therapy		Sulphamezathine Therapy (Oral)			Sulphamerazine Therapy (Oral)	Total
	Oral Administration 200,000 Units × 4	One Intramuscular Administration 200,000 Units Followed by 3 Oral Administrations	0·5 g. Initially 0·25 g. 6-hourly	0·25 g. Initially 0·125 g. 4-hourly With Penicillin Locally	0·5 g. Initially 0·25 g. 6-hourly With Penicillin Locally	0·5 g. Initially 0·25 g. 8-hourly	
Gonococcus							
Mild		—	4	—	—	—	4
Moderate		2	—	1	—	2	5
Severe		2	1	1	1	—	14
Staphylococcus aureus							
Mild		1	—	2		3	6
Moderate		2	2	3		3	10
Severe		1	1	2		2	6
Staphylococcus albus							
Mild	1	3	3	2		1	10
Moderate	1	3	4	4	3	2	17
Severe	—	2 (*a*)	2 (*b*)	1 (*c*)	—	1	6
Staphylococcus albus with diphtheroids							
Mild	—		2				2
Moderate			—				—
Severe			1				1
Diphtheroids							
Mild	—	1	1	—	—		2
Moderate	1	—	4	2	2		7
Severe	—	1 (*a*)	5 (*c*)	(*a*)	—		9 (*f*)
Other bacilli							
Mild	—	1	—	1	—		2
Moderate	1	1	2	1	1		6
Severe	—	3 (*a*)	3 (*a*)	4 (*b*)	—		12 (*d*)
Streptococcus viridans							
Mild			2		—		2
Moderate			1		1		2
Severe			—		—		4 (*a*)
Other coccal organisms							
Mild		1		1			2
Moderate		2		1			3
Severe		—		—			—
Negative without inclusion bodies							
Mild		—	8	—	2	2	12
Moderate		2	6	3	1	6	18
Severe		—	1	—	—	—	1
Negative with inclusion bodies							
Mild		—	5	—	—	1	6
Moderate		1	4	3	1	1	10
Severe		—	2	—	—	—	2
Total	4	26	57	30	10	24	151

(*a*) Inclusion bodies present in 1 case. (*c*) Inclusion bodies present in 3 cases. (*f*) Inclusion bodies present in 6 cases.
(*b*) " " " " 2 cases. (*d*) " " " " 4 " (*g*) " " " " 10 "

that by increasing the dose a rapid cure is obtained in a greater percentage of cases, but that the incidence of unsatisfactory response is uninfluenced.

3. *Combined Use of Sulphamezathine Orally and Penicillin Locally (40 Cases).*—A series of 30 cases were treated with sulphamezathine orally in the smaller dose combined with penicillin drops 10,000 units per ml., initially instilled at one-minute intervals for 30 minutes. A further 10 cases were treated with the larger dose of sulphamezathine and the same mode of penicillin locally. As can be seen from Table III, in both these small series the percentage of cases with rapid response was high (29 out of 40). For this series of 40 cases as a whole, the proportion of unsatisfactory responses is, however, once more not diminished. This is clearly so for the 30 cases treated with the smaller dose of sulphamezathine, whilst the 10 cases treated with the larger dose of sulphamezathine in combination with penicillin are too few to allow any definite conclusions to be drawn.

4. *Sulphamerazine Orally in an Initial Dose of 0.5 g. and a Maintenance Dose of 0.25 g. at Eight-hourly Intervals (24 Cases).*—In a series of 24 cases so treated, no fewer than 21 responded within one to three days, and the remaining three all cleared up within four to eight days, so that there was no case with an unsatisfactory response or relapse. Sulphamerazine had the further advantage that in none of these 24 cases was there any suggestion of intolerance, and the occasional cyanosis observed with sulphamezathine was entirely lacking.

5. *The Series as a Whole.*—Table IV brings out the salient features observed with the different modes of treatment in this series of 151 cases compared with the previously recorded result. If the small series of 24 cases treated by sulphamerazine is excluded it would seem that the methods recorded in the present study have failed to reduce the incidence of unsatisfactory responses and relapses. It is, however, clear that two conclusions can be confidently drawn regarding the use of penicillin and the sulphonamides. First, the intensive use of penicillin locally at one-minute intervals is still the best mode of applying

TABLE II.—*Comparative Results with Two Different Dosages of Sulphamezathine*

Dose		Total Cases	Clinical Cure in		Unsatisfactory Response or Relapse
Initial	Maintenance		1-3 Days	4-8 Days	
0·25 g. 4-hourly	0·125 g. 4-hourly	84	39·3%	44·0%	16·7%
0·5 g. 6-hourly	0·25 g. 6-hourly	57	68·4%	14·0%	17·6%

TABLE III.—*Results Obtained by the Combined Use of Sulphamezathine Orally and Penicillin Locally*

Mode of Treatment		Total No. of Cases	Cases Showing Clinical Cure in		Cases Showing Unsatisfactory Response
			1-3 Days	4-8 Days	
Sulphamezathine orally (*a*) 0·25 g. initial dose; 0·12 g. maintenance dose, 4-hourly	Penicillin drops 10,000 u/ml. Initially at 1-minute intervals for 30 minutes	30	20	1	9
(*b*) 0·5 g. initial dose; 0·25 g. maintenance dose, 6-hourly	" "	10	9	1	0

TABLE IV.—*Salient Features in the Present Series Set Against Main Results Previously Recorded*

	Total No. of Cases	Percentage of Cases Showing	
		Clinical Cure in 1–3 Days	Poor Responses or Relapses
Previous series:			
Sulphonamides orally (sulphapyridine, sulphamezathine, sulphadiazine, sulphathiazole, and sulphanilamide—0·25 g. initially and 0·125 g. 4-hourly)	333	32·4	16·3
Penicillin locally (drops, 2,500–10,000 units per ml., initially at 1-minute intervals) ..	104	74·0	26·0
Penicillin systemically (4 injections of 200,000 units at 3-hourly intervals) ..	39	84·4	15·6
Present series:			
Penicillin systemically (800,000 units)			
Oral administration	4	0·0	100·0
Combined intramuscular and oral administrations	26	57·7	42·3
Sulphamezathine orally:			
0·5 g. initially and 0·25 g. 6-hourly ..	57	68·4	17·6
0·25 g. initially and 0·125 g. 4-hourly, with penicillin locally	30	66·6	30·0
0·5 g. initially and 0·25 g. 6-hourly, with penicillin locally	10	90·0	0·0
Sulphamerazine:			
0·5 g. initially and 0·25 g. 8-hourly ..	24	87·5	0·0

penicillin in ophthalmia neonatorum. Secondly, the sulphonamides can with advantage be used in higher doses than those employed at present. A more rapid response is obtained if an initial dose of 0.5 g. is given, with a maintenance dose of 0.25 g. at six-hourly intervals with sulphamezathine and at eight-hourly intervals with sulphamerazine. As to the small series with sulphamerazine, the suggestion is that this drug may prove the sulphonamide of choice, possibly reducing the frequency of unsatisfactory responses and relapses as well as giving a high incidence of rapid results. The chance occurrence of a high proportion of these 24 cases being due to organisms readily susceptible to sulphonamides cannot, however, be excluded.

Therapeutic Failures

In the present series of 151 cases there were 34 which gave an unsatisfactory response or which relapsed; 15 of these were observed in the 30 cases treated with penicillin intramuscularly or orally. As this method of treatment was experimental and has proved unsatisfactory, these 15 cases need not be considered in any detail. It is enough to note that they did not contain an undue proportion of relatively resistant organisms.

Of the 121 cases treated by sulphamerazine or sulphamezathine with or without local penicillin 19 gave a poor response or relapsed. These 19 cases were observed in a series of 87 cases—the 57 treated by large doses of sulphamezathine orally and the 30 treated by sulphamezathine in smaller doses with penicillin locally. Seventeen of these 19 were relapses; in one case—completely negative bacteriologically—there was a persistent membranous cast of the conjunctiva, and in the remaining case diphtheroids, coliform bacteria, and inclusion bodies were present, leading to prolonged treatment but ending in a primary cure. Table V shows the clinical features of these 19 cases in comparison with the cases responding satisfactorily. It is clear that unsatisfactory response is not related to the degree of severity of the affection.

TABLE V.—*Degree of Severity in Cases with Satisfactory Response Compared with that seen in Cases with Relapse*

	Whole Series (121 Cases)	Series of 87 Cases	17 Cases with Relapse and 2 Cases with Slow Response
Mild	40	31	4
Moderate	62	41	10
Severe	19	15	5

Table VI sets out the data concerning causal organisms. It will be seen that the cases with unsatisfactory response are not confined to any one aetiological group. In all groups the satisfactory responses considerably outnumber the cases with relapse or slow response. It should, however, be noted that 10 out of the 19 cases showed inclusion bodies either alone or in combination with organisms. In the whole series of 121 cases inclusion bodies occurred either alone or in combination with organisms in 33 cases. There are therefore 10 failures out of 33 cases showing inclusion bodies, and nine failures in 88 cases without inclusion bodies. This confirms the previously recorded observation that cases with inclusion bodies are the most resistant to treatment. As the difficulty centres on relapse rather than on slow response, the question arises whether such cases should not be given a longer consolidation treatment than cases of ophthalmia neonatorum due to other exciting organisms.

TABLE VI.—*Distribution of Organisms in Cases with Satisfactory Response Compared with that seen in Cases with Relapse or Slow Response*

	Whole Series (121 Cases)	Series of 87 Cases	17 Cases with Relapse and 2 Cases with Slow Response
Gonococcus	10	7	2
Staphylococcus aureus	18‡	10†	2*
,, *albus*	23‖	16‖	3*
,, ,, with diphtheroids	3	3	1
Diphtheroids	7§	7§	3†
Other bacilli	8‡	7‡	3†
Streptococcus viridans	4*	3	—
Other coccal organisms	2	2	—
Negative, without inclusion bodies ..	29	18	1
,, with ,, ,, ..	17	14	4

* One case associated with inclusion bodies.
† Two cases ,, ,, ,, ,,
‡ Three cases ,, ,, ,, ,,
§ Four ,, ,, ,, ,, ,,
‖ Five ,, ,, ,, ,, ,,

Discussion

The present study suggests that the sulphonamides, used in larger doses than those advocated until now, tend to give results almost as rapid as those obtained by the intensive local use of penicillin. With larger doses of sulphonamides some 60 to 70% of cases of ophthalmia neonatorum give a clinical cure within one to three days. This is still less rapid than the results obtained with intensive local penicillin treatment, but not to any marked degree. Local penicillin therapy has the advantage that it can suppress pus formation within 20–30 minutes, whereas the sulphonamides take the better part of 24 hours to achieve this initial improvement. Sulphonamide therapy is, however, much simpler in application and is far less exacting on both the baby and the nurse.

When sulphonamides were first used in the treatment of ophthalmia neonatorum a dose of 0.125 g. initially and 0.062 g. at six-hourly intervals was given (Sorsby, Hoffa, and Smellie, 1942). Subsequently the maintenance dose was raised to 0.083 g. With these doses the incidence of unsatisfactory response and relapse was 38.1%. With the subsequent increase of the dose to 0.25 g. initially and 0.125 g. as a maintenance dose at four-hourly intervals this percentage fell to 16.3.

The higher dose suggested in the present study, whilst not influencing the relapse rate, has the merit of reducing the duration of treatment. This higher dose is innocuous and there is nothing to be gained by not adopting it as the standard dose for ophthalmia neonatorum. As between

sulphamezathine and sulphamerazine, the advantage seems to lie with sulphamerazine, though it has still to be proved that the frequency of relapses with this drug will be less than with sulphamezathine. Contrary to expectation, the combined use of penicillin locally and sulphonamide orally does not seem to reduce the relapse rate, but it should always be borne in mind that relapses are sometimes, possibly often, reinfections rather than relapses in the true sense.

Routine Procedure for Treatment

The steps in the two alternative methods of treating ophthalmia neonatorum available at present—sulphonamides orally and penicillin locally—may be thus summarized:

(*a*) *Steps in Common for the Two Methods.*—On admission a swab is taken for smear and culture and the eye is irrigated with half-normal saline at room temperature. A drop of adrenaline 1 in 1,000 is instilled and a scraping is taken from the palpebral conjunctiva for examination for the presence of inclusion bodies. Gutt. atropinae sulphas, 1%, are instilled if the cornea is affected. Any pus that may have accumulated is wiped away with moist pledgets of cotton-wool.

(*b*) *Procedure for Sulphonamide Treatment.*—(1) After the preliminary measures a tablet of sulphamerazine or sulphamezathine (0.5 g.) crushed into powder is given by mouth in a teaspoonful of water or milk. Alternatively a stock mixture can be used. (2) Sulphamerazine administration in doses of 0.25 g. is continued every eight hours. If sulphamezathine is used the administration has to be at six-hourly intervals. (3) Local treatment consists of three-hourly irrigation with saline solution during the first day in cases with profuse discharge; as a rule there is no need for further irrigation on the subsequent days. After irrigation medicinal paraffin is instilled as a precaution against the sticking together of the lids. (4) Atropine is instilled three times daily in cases with corneal haze or ulceration. (5) Sulphonamide administration is continued for 48 hours after clinical cure.

With this treatment swelling of the lids generally subsides within 12 hours after admission; purulent discharge disappears within 24 hours.

(*c*) *Procedure with Local Penicillin Therapy.*—(1) The preliminary measures are completed by the instillation of a drop of penicillin in a concentration of 10,000 units per ml. into the conjunctival sac. (2) The baby is now placed on the nurse's lap, while another nurse sitting near by instils one drop of penicillin solution, 10,000 units per ml., every minute for 30 minutes. Irrigation is not needed, as pus does not form to any extent; such thin mucoid discharge as is present can be ignored or, if it clings to the lid margin, wiped away with moist pledgets of cotton-wool. (3) At the end of this time there is invariably no pus and generally little or no discharge. The eye, however, is still moist, the lids are still swollen, and the lid margins tend to be sticky. The baby is returned to its cot, and instillation of penicillin drops is continued six times at five-minute intervals, followed by a similar number of instillations at half-hourly, hourly, and two-hourly intervals. This gives a total of 22 hours' treatment. Many cases require no further attention. (4) In some babies the lid margins still tend to remain sticky. It is advisable in such cases to continue with penicillin at two-hourly intervals until the eye is dry, when treatment is carried on for a further 12 hours.

Crystalline penicillin only should be used for making up the drops. Impure penicillin is likely to cause irritative reactions.

Summary

A series of 151 cases of ophthalmia neonatorum treated by several different methods is recorded.

Oral administration of doses of 200,000 units of penicillin, either exclusively or after an initial intramuscular injection, has proved disappointing.

Combined oral sulphonamide and local penicillin therapy proved effective in reducing the duration of treatment but ineffective in reducing the considerable frequency of relapses seen with either sulphonamide or penicillin therapy.

Duration of treatment was likewise reduced by increasing the dose of sulphonamide. With sulphamezathine, 0.5 g. initially and a maintenance dose of 0.25 g. six-hourly, some 70% of cases showed clinical cure within one to three days. Similar results were obtained with sulphamerazine, 0.5 g. initially and 0.25 g. at eight-hourly intervals. The use of these larger doses of sulphonamide does not apparently influence the relapse rate; it is, however, possible that sulphamerazine may prove to be a favourable exception.

For the present the best way of administering penicillin is still the instillation of drops of 10,000 units per ml. initially at intervals of a minute for half an hour and subsequently at less frequent intervals. For the best results with sulphonamide therapy higher doses than those used previously are necessary.

We are indebted to the matron of White Oak Hospital and Sister Condon, of the Ophthalmia Neonatorum Unit, for their loyal help in the treatment of the cases recorded here.

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BACTERIOPHAGE TYPES IN PENICILLIN-RESISTANT STAPHYLOCOCCAL INFECTION

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Many studies concerning the incidence of penicillin-resistant staphylococcal infection have been reported, and it is now generally agreed that this is increasing (Spink *et al.*, 1944, 1945; Bondi and Dietz, 1945; Gallardo, 1945; Plough, 1945; Harley *et al.*, 1946; Barber and Rozwadowska-Dowzenko, 1948). Results of investigations of a series of infections occurring in a single hospital, however, are difficult to assess, as such institutions often seem to be breeding-grounds of a particular strain of pathogenic staphylococcus. Thus in previous studies in a single hospital by one of us (Barber, 1947a, 1947b; Barber and Rozwadowska-Dowzenko, 1948) it was found that 59 of 100 cases of staphylococcal infection investigated in 1948 yielded penicillin-resistant staphylococci, whereas the incidence in a similar series was 38% in 1947 and 14.1% in 1946. Each year, however, it was found that a significantly high proportion of the penicillin-resistant strains when typed by the bacteriophage method fell into the 6/47 group, suggesting that most of the penicillin-resistant infections might have been caused by a single strain of staphylococci.

Recent experience, however, has led us to the conclusion that a large number of penicillin-resistant staphylococci isolated from infections in widely separated hospitals belong to the 6/47 phage group. In the present investigation, therefore, staphylococci isolated from a series of 100 cases of infection occurring in this hospital have all been tested for penicillin sensitivity and phage-typed to see if the two could be correlated.

Methods

During the investigation all cultures of staphylococci (usually on blood-agar plates) obtained from cases of infection were collected from the routine laboratory. From each primary plate 10 colonies were picked off and streaked on to penicillin ditch-plates, the ditch containing 10 units of penicillin per ml. The remaining growth was then emulsified in broth and plated out on a similar penicillin ditch-plate in order to detect small numbers of penicillin-resistant organisms which might otherwise have been missed. After incubation overnight the plates were examined. If all colonies from a single specimen showed a similar reaction to penicillin one was picked off into "lemco" broth for further investigation. If penicillin-sensitive and penicillin-resistant staphylococci were present, one colony of each was similarly picked off.

All staphylococci were tested for coagulase by the slide method and only coagulase-positive strains included in the series. Later all strains in the series were tested for haemolysin production by the method of Gillespie and Simpson (1948), and strains giving doubtful or negative results were tested for coagulase production by the tube method of Fisk (1940) and for haemolysin by the method described by McFarlan (1938).

All penicillin-resistant strains were tested for penicillinase production by the method described by Barber (1947a); 17 of them were tested by the serial dilution method in broth, using two different-sized inocula in each case, as recommended by Gilson and Parker (1948). Sensitivity to streptomycin was also tested on ditch-plates, the ditch containing 100 units of streptomycin per ml., and to sulphonamides on ditch-plates made of laked horse-blood agar as recommended by Harper and Cawston (1945), the ditch containing 1 in 5,000 sulphathiazole. All ditch-plates, whether for testing penicillin, streptomycin, or sulphonamide sensitivity, were kept for 24 hours before use to allow diffusion of the chemotherapeutic agent, and part of every ditch-plate was seeded with the Oxford staphylococcus as a control. Phage-typing of all strains was carried out by the method now used at the Central Public Health Laboratory, using the same 25 filtrates. The method is based on the work of Wilson and Atkinson (1945).

Penicillin Sensitivity

Specimens were examined from 100 consecutive patients with infection due to coagulase-positive staphylococci (hereafter referred to as *Staph. pyogenes*). The results are given in Table I, in-patients and out-patients being separated. From 35 patients penicillin-resistant strains of *Staph. pyogenes* were isolated: from 24, all colonies tested were resistant to penicillin; from 11, sensitive and resistant colonies were isolated in each case from a single specimen. Thus 111 strains of *Staph. pyogenes* were obtained from 100 specimens. The difference between sensitive and resistant strains was clear-cut in every instance. All the penicillin-resistant colonies when streaked across the penicillin ditch-plates grew at least to the ditch, whereas the sensitive colonies showed an area of inhibition similar to that shown by the Oxford staphylococcus. It will be seen from Table I that the incidence of resistant strains was greater in in-patients than in out-patients. The results, analysed according to type of infection, are shown in Table II.

TABLE I.—*Analysis of Patients Yielding Staph. Pyogenes in Relation to Penicillin Sensitivity*

Aug.–Dec., 1948	No. of Patients	Patients with Penicillin-resistant Strains		
		All Colonies Resistant	Sensitive and Resistant Colonies Isolated	Total
In-patients ..	49	13	7	20
Out-patients ..	51	11	4	15
Total ..	100	24	11	35

TABLE II.—*Results According to Type of Infection*

Type of Infection	Total Patients	Patients Yielding Resistant Strains
Carbuncles, abscesses, boils, etc.	53	14
Superficial skin lesions	19	9
Infected wounds	5	3
Pulmonary	8	4
Conjunctival	4	2
Aural	1	—
Nasopharyngeal	4	—
Genito-urinary	5	3
Inadequate information	1	—
	100	35

Previous treatment with penicillin was studied to see if this had any relation to the incidence of resistant strains. In only 67 of the patients was information regarding penicillin treatment available. Penicillin sensitivity in relation to treatment within the preceding three months in this group is shown in Table III.

TABLE III.—*Relation of Previous Treatment to Incidence of Resistant Strains*

	Penicillin Treatment within Previous 3 Months	No Penicillin Before Specimen Taken
Penicillin-sensitive strains only isolated ..	19	22
Penicillin-resistant strains isolated ..	22	8
Penicillin-sensitive and penicillin-resistant strains isolated	3	6

It will be seen that 22 of 41 patients who had been treated with penicillin yielded penicillin-resistant staphylococci, whereas only eight of 30 patients not treated with penicillin yielded such strains. One patient with an axillary abscess had a specimen taken before receiving any penicillin, and this yielded a very few colonies of penicillin-resistant and a heavy growth of penicillin-sensitive *Staph. pyogenes*. Treatment with penicillin was then started, and three weeks later a specimen of pus was received which yielded a heavy growth of *Staph. pyogenes*, and all colonies tested were penicillin-resistant.

The incidence of penicillin-resistant strains was correlated with length of hospital treatment in 46 cases, and the figures are given in Table IV. It will be seen that only 4 out of 22 patients who had been attending the hospital for a week or less yielded penicillin-resistant strains, whereas 10 of 18 patients who had been attending for a fortnight or more yielded such organisms.

TABLE IV.—*Incidence of Penicillin-resistant Strains of Staph. Pyogenes in Relation to Length of Treatment in this Hospital*

No. of Days under Treatment	Patients Yielding			Total
	Penicillin-sensitive Colonies Only	Penicillin-resistant Colonies Only	Sensitive and Resistant Colonies	
0	14 (4)	2 (1)	1 (1)	17 (6)
1–7	4 (2)	1	0	5 (2)
8–14	3 (3)	1	2	6 (3)
15–28	3 (1)	7 (1)	0	10 (2)
Over 28 ..	5 (5)	3 (1)	0	8 (6)
Total ..	29 (15)	14 (3)	3 (1)	46 (19)

The figures in parentheses refer to the number of out-patients in each group.

Degree and Type of Resistance to Penicillin

All 35 penicillin-resistant strains destroyed penicillin. As is now well recognized (Luria, 1946 ; Barber, 1947a) the degree of resistance of such organisms when measured in the laboratory may vary many hundredfold according to the size of inoculum used. It is therefore extremely difficult to devise a test giving accurate information on the degree of resistance which will help the clinician in deciding the probable effect of penicillin in a particular case of infection. Gilson and Parker (1948) have suggested that the double sensitivity test in broth, using two different-sized inocula, is the most informative, as the results obtained are directly related to the degree and rate of penicillinase production. This test was carried out on 17 of the resistant strains of *Staph. pyogenes* isolated in this series (Table V). It will be seen that a large inoculum was

TABLE V.—*Showing Degree of Resistance*

Greatest Concentration of Penicillin Permitting Growth		No. of Strains
Large Inoculum (Approx. 1,000,000 orgs.)	Small Inoculum (Approx. 1,000 orgs.)	
50 u./ml. or more	1–4 u./ml.	7
50 „ „	0·25–0·5 u./ml.	5
25 „	1 u./ml.	1
25 „	0·25–0·5 u./ml.	2
12·5 „	0·25 u./ml.	1
12·5 „	0·03 u./ml.	1
0·03 „	0·03 u./ml.	Oxford Staphylococcus

able to grow in from 12.5 to 50 units per ml., whereas a small inoculum was able to grow only in from 0.03 to 4 units per ml.

Phage-typing

All the 111 strains of *Staph. pyogenes* were phage-typed, and the results in relation to penicillin sensitivity are given in Table VI. Cultures reacting with one or more closely

TABLE VI.—*Phage Groups of 111 Strains of Staph. Pyogenes Isolated in Present Series*

Phage Group	No. of Strains of *Staph. pyogenes*	
	Penicillin-sensitive	Penicillin-resistant
6/7/47	9	24
52A	18	4
3	16	0
42	5	0
29/31/52	6	0
44	1	0
Non-typable	21	7
Total	76	35

related phages have been grouped together, and the strains in a particular group do not all give identical reactions. Of those classified as 6/7/47 nearly all reacted strongly with phage 47, and many also reacted with various combinations of 6, 7, and 3298. A few strains included in this group were sensitive to phage 6 or phage 7 only. Group 29/31/52, again, consists of strains showing varying reactions with one or more of these three phages. Nearly all the strains classified as 3 were sensitive to only one of the phages 3A, 3B, and 3C, and similarly strains in the 42 group reacted only with one of the phages 42B, 42C, 42D, and 42E. Apart from trace reactions, the 52A strains reacted with this phage alone. The non-typable group consists mainly of strains giving no reactions, but includes a few which were very sensitive and could not be classified.

It will be seen from Table VI that of the 35 penicillin-resistant strains as many as 24 fell into the 6/7/47 group, and that the only other typable strains belong to type 52A. The penicillin-sensitive strains, on the other hand, were distributed among all the groups, only nine out of 76 belonging to group 6/7/47.

As mentioned above, penicillin-sensitive and penicillin-resistant strains were isolated from the same patient in 11 cases. These 11 pairs of strains were phage-typed and the results are given in Table VII. In nine of the 11 pairs the

TABLE VII.—*Phage Types of Pairs of Strains Isolated from the Same Patient*

Patient	Phage Type of Strain of *Staph. pyogenes*	
	Penicillin-sensitive	Penicillin-resistant
5	N.T.	6*
10	47*	N.T.
12	N.T.	N.T.
32	42E	47*
40	N.T.	47*
41	N.T.	7*
46	N.T.	52A
63	52A	6/47*
75	N.T.	6/47*
82	52A	52A
92	42E	N.T.

N.T. = Non-typable. * Side-reactions.

two appear to be different in phage-type, but it is unfortunate that in eight cases one of the pair is non-typable. From one of these 11 patients penicillin-resistant and penicillin-sensitive strains of *Staph. pyogenes* were isolated from both the lesion (sycosis barbae) and the nose. From each site the penicillin-resistant strain was phage type 6/47 and the penicillin-sensitive strain non-typable.

It occurred to us that the apparent correlation of penicillin resistance and phage group 6/7/47 might be a purely local phenomenon. A number of penicillinase-producing strains of *Staph. pyogenes* isolated from patients in widely separated hospitals were therefore collected together and phage-typed. The cultures from Hammersmith Hospital and the General Lying-In Hospital, S.E.1, were already in our possession, and the cultures from Canterbury, Manchester, and the West London Hospital were kindly sent by Dr. Forbes, Dr. Martyn, and Dr. Morris respectively. Except for the cultures from Manchester, which were isolated from healthy infants, all strains came from cases of infection. The results are given in Table VIII.

TABLE VIII.—*Phage Types of Penicillin-resistant Strains of Staph. Pyogenes Isolated from Patients*

Phage Group	Source						Total
	Hammersmith Hospital	St. Thomas's Hospital	General Lying-in Hospital, S.E.1	West London Hospital	Kent and Canterbury Hospital	St. Mary's Hospital, Manchester	
6/7/47	25	27	0	1	27	5	85
52A	1	4	15	0	1	0	21
42	3	0	0	0	0	0	3
3	1	0	0	0	0	0	1
29/31/52	1	0	0	0	0	0	1
N.T.	3	8	13	0	4	1	29
Total	34	39	28	1	32	6	140

In all, 140 strains were tested and as many as 85 (61%) fell into the 6/7/47 group. Apart from non-typable strains the only other large group is 52A. This is mainly due to an outbreak of infection among the babies at the General Lying-In Hospital which at the time of writing is under investigation. Nearly all the infections occurring at present in this maternity hospital are due to penicillinase-producing *Staph. pyogenes* and, as will be seen in the table, most of the strains are phage type 52A. A very large number of nurses in the hospital are carrying a similar organism in the nose.

Streptomycin and Sulphonamide Sensitivity

All 111 strains were tested for sensitivity to streptomycin and sulphonamides. The results are presented in relation to penicillin sensitivity in Table IX. All strains showed a sensitivity to streptomycin comparable to that of the Oxford staphylococcus. One of the patients, who had a lung abscess infected with penicillin-resistant *Staph. pyogenes*, *Proteus*, and non-haemolytic streptococci, was subsequently treated with streptomycin. Within five days the *Staph. pyogenes* had become highly resistant to this antibiotic.

TABLE IX.—*Streptomycin and Sulphathiazole Sensitivity of 111 Strains of Staph. Pyogenes*

	Penicillin-sensitive	Penicillin-resistant	Total
Streptomycin-sensitive ..	76	35	111
Streptomycin-resistant ..	0	0	0
Sulphathiazole-sensitive ..	72	18	90
Sulphathiazole-resistant ..	4	17	21

Twenty-one of the 111 strains were considerably more resistant to sulphathiazole than the Oxford staphylococcus, and 19 of these strains grew at least to the edge of the ditch containing 1 in 5,000 sulphathiazole. It is interesting that 17 of the 21 sulphathiazole-resistant strains were also penicillin-resistant. Eight of the patients yielding sulphonamide-resistant strains had had some form of sulphonamide treatment before the specimen was taken, eight had not, and from five information in relation to treatment is not available.

α-Toxin Production

The strains isolated in the present series were all coagulase-positive on testing by the slide method. As Schwabacher, Cunliffe, Williams, and Harper (1945) and Christie, North, and Parkin (1946) have suggested that the production of α-lysin is more closely correlated with pathogenicity than coagulase production, all the strains were examined for α-toxin production, using the sheep-blood plate method of Gillespie and Simpson (1948). Of the 111 strains, 101 were α-toxigenic, two were negative, and eight were regarded as giving doubtful reactions. The negative and doubtful strains were tested for coagulase by the tube method of Fisk (1940) and found to be positive. The doubtful reactions on the sheep-blood agar plates were due in some instances to the simultaneous production of β-toxin in amounts sufficient to mask the appearances due to the α-toxin. On testing the eight doubtful strains for the production of α-toxin in broth, using the method of McFarlan (1938), four were found to be positive, while the remaining four were negative, as also were the two strains found to be negative by the sheep-blood plate method. Thus of the 111 coagulase-positive strains 105 were α-toxigenic.

Of the non-toxigenic strains, three belonged to phage type 3C; the remainder were non-typable.

Discussion

It is remarkable that such a high proportion of penicillin-resistant strains of *Staph. pyogenes*, isolated from patients in widely different hospitals, should belong to phage group 6/7/47. While in the present state of our knowledge it is possible only to speculate on the meaning of this, it may well be of considerable epidemiological importance. It is possible that strains of phage group 6/7/47 are genetically less stable than those of other phage groups, and have thus given rise to penicillin-resistant mutants more readily. A significant number of the remaining penicillin-resistant strains were type 52A, but nearly all these were isolated from neonatal infections occurring in a single maternity hospital over a period of three months. It is interesting that *Staph. pyogenes* of phage type 52A has been isolated from the noses of many nurses in this maternity hospital, and that some of the strains are sensitive to penicillin whereas others are resistant. It is possible that an originally sensitive strain of *Staph. pyogenes* carried in this hospital has recently given rise to a penicillin-resistant mutant which has now established itself there.

The ultimate origin of penicillin-destroying strains of *Staph. pyogenes* is still undecided. Spink and Ferris (1947) favour the hypothesis that such strains arise as mutants from penicillin-sensitive organisms. The work of Barber (1949) on the readiness with which, *in vitro*, penicillinase-producing staphylococci give rise to penicillin-sensitive variants supports this theory. Penicillin-destroying mutants, however, cannot be induced by growing penicillin-sensitive strains of *Staph. pyogenes* in penicillin *in vitro*. Spink *et al.* (1945, 1947) claim that such a change may be induced *in vivo* by penicillin treatment. As, however, their strains of *Staph. pyogenes* were not typed, it is possible that they were dealing with mixed infections due to penicillin-sensitive and penicillin-resistant strains of different types; that the latter, initially in the minority, were favoured at the expense of the former, and thus by a simple process of selection ultimately supplanted the penicillin-sensitive organisms.

Such mixtures of penicillin-sensitive and penicillin-resistant strains of *Staph. pyogenes* have now been isolated from the same patient on many occasions, and in most cases where such pairs have been phage-typed they have been found to give different reactions. Of 11 such pairs in the present series nine gave different phage reactions, and it seems likely that they were different phage types, although it is impossible to be quite certain of this where one of the pair was non-typable. In previous studies (Barber, 1947a, 1947b; Barber and Rozwadowska-Dowzenko, 1948) 10 such pairs were phage-typed and eight pairs were shown to be of different types.

Whatever the ultimate origin of penicillin-destroying strains of *Staph. pyogenes*, it seems likely (Barber and Rozwadowska-Dowzenko, 1948) that selection plays a large part in the increasing incidence of such strains in hospitals. The work of Harley *et al.* (1946) and Forbes (1949) further makes it clear that the incidence of penicillin-resistant strains isolated from staphylococcal infections in hospital in-patients is much greater than that in out-patients. In the present study it will be seen that 20 of 49 in-patients yielded penicillin-resistant strains compared with 15 of 51 out-patients, and that there was a significantly higher incidence of penicillin-resistant organisms in patients who had been under hospital treatment for more than a fortnight.

Kirby (1944) first pointed out that penicillin-resistant strains of *Staph. pyogenes* isolated from infective processes were characterized by the production of a powerful penicillin-inactivator. Since then Spink, Hall, and Ferris (1945), Bondi and Dietz (1945), Gots (1945), Barber (1947a, 1947b), Barber and Rozwadowska-Dowzenko (1948), Martin and Whitehead (1949), Martyn (1949), and Forbes (1949) have recorded studies in which all penicillin-resistant strains of *Staph. pyogenes* isolated from cases of infection or human carriers were shown to destroy penicillin. The resistant strains isolated in the present series likewise have this property.

Luria (1946) and Barber (1947a) have both shown that the degree of resistance of penicillinase-producing organisms recorded in the laboratory was dependent on the size of inoculum used. In the present series it will be seen (Table V) that with many strains a small inoculum was

sensitive to less than 1 unit of penicillin per ml., whereas a large inoculum grew in from 12.5 to 50 units per ml. Thus the heaviness of the infection is the most important factor in deciding whether a patient infected with such an organism will benefit by penicillin treatment. As it is usually impossible to determine this, elaborate laboratory tests designed to show degree of sensitivity or rate of penicillinase production are valueless. It should further be emphasized that where a small inoculum is used in testing penicillin sensitivity the type of resistant organism here described may easily be missed.

The differentiation of pathogenic from non-pathogenic staphylococci in the laboratory has received considerable attention lately. Schwabacher, Cunliffe, Williams, and Harper (1945) and Christie, North, and Parkin (1946) found a small number of strains which were coagulase-positive but did not produce α-lysin, and both sets of workers considered the latter test to be more closely correlated with pathogenicity. In the present investigation all 111 strains were coagulase-positive and 105 were α-toxigenic. Although no evidence could be obtained to indicate that the α-lysin-negative strains were less pathogenic than the others, none of them came from very serious cases of infection.

Summary

Out of 100 cases of infection with *Staph. pyogenes* occurring in this hospital 35 yielded penicillin-resistant strains. In 24 cases all colonies tested were penicillin-resistant and in 11 both sensitive and resistant strains were isolated.

All penicillin-resistant strains were shown to destroy penicillin. Seventeen were tested for penicillin sensitivity, using two different-sized inocula, and it was found that whereas a small inoculum was sensitive to from 0.06 to 4 units per ml. a large inoculum grew in from 12.5 to 50 units per ml.

Twenty-four of the 35 penicillin-resistant strains were shown to belong to phage group 6/7/47, whereas only nine of 76 penicillin-sensitive strains fell into this group. When 140 penicillin-resistant strains isolated from patients in a variety of hospitals were phage-typed, 85 were found to belong to the 6/7/47 group.

All strains were initially sensitive to streptomycin. A strain from one patient became resistant after five days' treatment with this antibiotic.

Twenty-one of the 111 strains were resistant to sulphathiazole, and 17 of these were also resistant to penicillin.

All 111 strains were coagulase-positive; 105 were α-toxigenic.

We are grateful to Dr. R. E. O. Williams and the staff of the Staphylococcal Reference Laboratory for teaching us to phage-type staphylococci and for supplying us with a set of filtrates. We should also like to thank Dr. J. Bamforth and the staff of the Jenner Laboratory for supplying us with the specimens on which this work was based, Dr. Bhatia for assistance with some of the penicillin-sensitivity tests, and Dr. Forbes, Dr. Martyn, and Dr. Morris for sending us cultures of penicillin-resistant *Staph. pyogenes*.

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INFECTION WITH PENICILLIN-RESISTANT STAPHYLOCOCCI IN HOSPITAL AND GENERAL PRACTICE

BY

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The isolation of penicillin-resistant staphylococci from clinical sources, at one time a rare event, is now a commonplace. The great majority of these strains possess a natural resistance to penicillin by virtue of their ability to produce a penicillin-neutralizing enzyme, penicillinase (Kirby, 1944; Bondi and Deitz, 1945). Some indication of the frequency with which penicillinase-producing staphylococci are encountered in hospital practice, and the rising proportion of staphylococcal infections due to these strains, can be gauged from the work of Barber, who recorded a progressive increase in the incidence of infections with resistant strains from 14.1% in 1946 to 59% in 1948 (Barber, 1947a, 1947b; Barber and Rozwadowska-Dowzenko, 1948).

Dr. Barber's work has aroused much interest and not a little alarm, for at first sight it might appear that the power of penicillin in combating staphylococcal infection is decidedly on the wane. However, the results of an investigation carried out in a large hospital are not necessarily representative of the community as a whole, an opinion to which Dr. Barber herself subscribes when she states (Barber and Rozwadowska-Dowzenko, 1948): "Though penicillin-resistant strains of *Staph. pyogenes* are now appearing with increasing frequency in many hospitals, this is probably not the case in the community at large." This statement receives substantiation from the results of an investigation carried out at this hospital during the past 12 months.

Outline of Investigation

Staphylococci isolated on routine culture were in the first instance tested for coagulase-production by the method of Gillespie (1943) and sensitivity to penicillin on ditch-plates, using 10 units of penicillin per ml. of agar in the ditch. Coagulase-positive strains were then subcultured and set aside for further investigation, including a quantitative estimation of penicillin sensitivity (using serial dilutions of penicillin in 1-ml. amounts of broth and an inoculum of 0.02 ml. of a 1 in 100 dilution of a 24-hour broth culture), production of penicillinase, and sensitivity to streptomycin.

In the meantime further information regarding the source of the specimens which yielded coagulase-positive staphylococci was obtained by questioning patients and nursing staff, and in some cases examining the lesions from which the specimens were obtained. In particular it was noted whether the patient was an in-patient or out-patient not only at the time the specimen was collected but also at

the time that infection first became apparent, and whether the patient was having or had had penicillin treatment. Finally, attention was paid to the nature of the specimens submitted for examination, and to the amount and purity of growth on primary isolation, with a view to ensuring that the staphylococci were both pyogenic and truly pathogenic. As one would expect from the mode of selection, the great majority of strains accepted for analysis were from specimens of frank pus or purulent material from boils, abscesses, septic fingers, infected wounds, etc., and in nearly all cases the growth of staphylococci on primary culture was heavy and pure.

Analysis of 120 Strains of Staph. pyogenes

One hundred and twenty strains of *Staph. pyogenes* from the same number of patients were investigated. All but three were of the aureus variety; the three albus strains were strongly coagulase-positive on repeated examination, were present in pure culture on primary isolation, and the source of the strains left no doubt that they had been actively pathogenic. Of these 120 strains 73 (60.8%) were sensitive to penicillin and 47 (39.2%) resistant. The sensitive strains possessed a degree of sensitivity approximately equal to that shown by the control Oxford staphylococcus, and none produced penicillinase. On the other hand, all the resistant strains were penicillinase-producers. The resistance was gross in all cases both when tested on the ditch-plate (growth extending up to and over the ditch) and when estimated quantitatively, the minimal concentration of penicillin required to inhibit growth varying from 5 to 400 times that required to inhibit the control strain of Oxford staphylococcus (Table I).

TABLE I.—*Degree of Resistance of 41* Resistant Strains*

	Inhibiting Concentration of Penicillin in Units per ml.							
	32	16	8	4	2	1	0·8	0·4
No. of strains	1	3	5	9	7	2	6	8

* Six strains were not available for quantitative sensitivity tests. *Staph. aureus* (Oxford) was inhibited by 0·08 unit per ml.

Resistance to streptomycin was not encountered among any of these 120 strains, all possessing a sensitivity to this antibiotic of the same order as the control Oxford staphylococcus.

Analysis of 78 Out-patient and In-patient Strains

A separation of the 120 strains into those derived from out-patients and those from in-patients was then attempted. Inevitably a number of strains could not be placed in either of these categories. Thus a specimen may have been received from an in-patient, but the history of the case indicated that infection had occurred before the patient was admitted to hospital. Conversely, an out-patient may have given a history of a recent stay in hospital for the treatment of the condition from which he was suffering at the time the out-patient specimen was collected. Such cases in which the origin of the infecting strain was not clearly established have been omitted from this part of the analysis. Altogether 42 strains were unclassifiable, leaving a total of 78 strains which could be labelled with confidence "out-patient" or "in-patient" strains. The incidence of sensitive and resistant strains for this reduced series was 60.25% and 39.75% respectively, indicating that the exclusion of these 42 unclassifiable strains had not resulted in any significant deviation from the ratio for the original series, which was 60.8% sensitive to 39.2% resistant.

Out-patient Series.—The 40 strains which comprised the out-patient group were derived from specimens collected in the casualty and out-patient departments of this and neighbouring hospitals, and from specimens sent in by local practitioners. All but five of these strains were highly sensitive to penicillin, representing an incidence of sensitive strains of 87.5% and of resistant 12.5% (Table II).

TABLE II.—*Incidence of Penicillin-resistant Staph. pyogenes from 78 Patients with Staphylococcal Infection*

Source	No. of Strains	Resistant Strains
Out-patients	40	5 (12·5%)
In-patients	38	26 (68·4%)

In-patient Series.—Strains accepted for this series were recovered from patients whose infection had arisen during their stay in hospital. Thus infected operation wounds, infected plaster sores and bedsores, and neonatal infections were among the lesions which yielded in-patient strains. Of the 38 strains in this group no fewer than 26 (68.4%) were resistant, and 12 (31.6%) were sensitive. When these resistant strains were further analysed it was found that 11 of the 26 had originated in one department of the hospital, the maternity unit. This finding prompted a search for a carrier among the staff of the unit, and one of the senior nurses was found to be a persistent heavy nose-and-throat carrier of a penicillin-resistant coagulase-positive *Staph. aureus*. Phage-typing of eight patient strains, two carrier strains, and three strains isolated from the ward dust by exposing blood-agar plates was carried out through the courtesy of Dr. R. E. O. Williams at the Central Public Health Laboratory, Colindale. The results (Table III) show

TABLE III.—*Phage Reactions of Resistant Strains from Maternity Unit*

Ref. No.	Source	Phage Reaction	Remarks
50	Pemphigoid impetigo. Pustular rash	3A	
73	Ophthalmia neonatorum ..	3A	
77	Pustules on nipple	3A	
87	,, ,, ,, ...	47+	
94	Ophthalmia neonatorum ..	3A	
95	Pustular rash. Pemphigoid impetigo	47+	Child of No. 101
101	Pustular rash	47/47B+	Mother of No. 95
108	Ophthalmia neonatorum ..	47/47B+	
49	Nose and throat of Nurse 1 ..	3A	Heavy persistent carrier
78	Nose and throat of Nurse 2 ..	52A	Temporary carrier
79	Ward dust, Colony 1	3A	
80	Ward dust, Colony 2	7	
97	Ward dust, Colony 3	47/47B+	

that all of the patients were infected with staphylococci belonging to one of two phage-types, that these same types were isolated from the ward dust, and that one of them (type 3A) was carried by a member of the nursing staff.

Effect of Previous Penicillin Therapy on the Resistance Rate

A history of treatment with penicillin for several days before the collection of the specimens was obtained from 41 patients. Twenty-five strains from these penicillin-treated patients were resistant and 16 were sensitive. Of 51 strains from patients not treated with penicillin 22 were resistant and 29 sensitive (Table IV). In short, the incidence

TABLE IV.—*Penicillin Therapy and Resistance Rate*

Source*	No. of Strains	Resistant Strains
Untreated patients	51	22 (42%)
Treated patients	41	25 (59%)

* The 92 patients which comprise this series include both out-patients and in-patients, and are independent of those quoted in Table II.

of resistant strains was slightly but not significantly higher in patients receiving penicillin.

In interpreting these findings it should be remembered that 42 of the 47 resistant strains were hospital strains, and, although they were isolated from 42 patients, it cannot be said that they were all distinct strains, for, as phage-typing has shown, dissemination of any one strain or the descendants of that strain by means of cross-infection had probably occurred to some extent. Consequently a number of the infecting strains were already resistant before the institution of penicillin treatment. All five out-patients and 20 in-patients from whom resistant strains were isolated were on large doses of penicillin when the specimens were collected. It is conceivable that the cells of the original infecting strain were for the most part susceptible, but that a number of variants within the strain enjoyed a measure of resistance. By the time the specimens were collected penicillin had eliminated the susceptible cocci, leaving a flora which was resistant.

Discussion

There is no doubt that staphylococcal infections due to penicillin-resistant strains are being encountered with increasing frequency in hospital practice. The reason for this unwelcome trend would seem to lie in the fact that the staphylococcal population of most hospitals at the present time is dominated by strains which possess a natural resistance, the inevitable consequence of the widespread use of penicillin during the past few years. By a process of natural selection these resistant strains have survived and propagated at the expense of susceptible breeds; and their presence in ward dust and the upper respiratory passages of members of the hospital staff, together with case-to-case infection, no doubt accounts for the high incidence of this type of infection in hospitals. By contrast, the environmental conditions which prevail in the community at large offer small scope for the perpetuation and dissemination of resistant strains, and one would anticipate a much lower incidence of infection due to these strains among the general population.

The carrier rate of penicillin-resistant staphylococci among hospital and non-hospital employees is under investigation and will be the subject of a later communication. Preliminary findings indicate that the rate of carriage of these strains by members of the staff of this hospital is disturbingly high. Of 50 ward nurses no fewer than 23 (46%) were found to carry in their anterior nares coagulase-positive *Staph. aureus* resistant to at least 1 unit of penicillin. The resistant strains all produced penicillinase. Of a control group of 50 office workers (not attached to the hospital) only one (2%) was found to be a nasal carrier of a penicillin-resistant strain.

From these and other observations one might attempt a grouping of staphylococcal infections according to the sensitivity to penicillin of the infecting strains, as follows. (*a*) Infection due to a pure sensitive strain the cells of which are all susceptible to the action of penicillin in adequate dosage. The majority of infections, especially those met with in general practice, fall into this group. (*b*) Infection due to a pure resistant strain—for example, hospital infection—which is naturally resistant to penicillin. (*c*) Infection due to a single strain, for the most part sensitive but containing a variable number of naturally resistant penicillinase-producing variants. Under the influence of penicillin such a strain may develop into a pure resistant strain owing to the elimination of penicillin-susceptible cells (Anderson *et al.*, 1944; Spink and Ferris, 1947). (*d*) Infection due to a sensitive staphylococcus complicated by superinfection with an insensitive strain of different phage type (Barber, 1947a, 1947b).

Recent reports on the high incidence of resistant strains have cast doubt on the competence of penicillin to deal with staphylococcal infections (leading article, *British Medical Journal*, 1947, **2**, 874). The results of this study are presented in the hope of restoring confidence in penicillin for the treatment of staphylococcal infections in general practice. So far as the results of a limited study confined to one provincial hospital area are applicable to the general situation, it would seem that intelligent therapy with penicillin (and other measures when indicated) should effect a cure in nine of ten out-patients with staphylococcal sepsis. At the same time the results confirm the high proportion of hospital infections due to resistant strains: only one in every three patients with infection contracted during their stay in this hospital was eligible for penicillin therapy.

Penicillinase-producing strains of staphylococci are fully pathogenic (North and Christie, 1946; Barber, 1947a) and on occasion are capable of causing severe and sometimes fatal infections, such as staphylococcal septicaemia. Since resistance to penicillin appears to be specific, and not necessarily accompanied by resistance to either sulphonamides (Spink, Hall, and Ferris, 1945) or streptomycin, recourse may be had to one or both of the latter anti-staphylococcal agents in the treatment of severe infections due to penicillin-resistant staphylococci.

Summary

Seventy-eight strains of *Staph. pyogenes* from clinical sources have been analysed according to their sensitivity to penicillin. The resistance rate of strains derived from out-patients was 12.5% and from in-patients 68.4%.

All resistant strains produced penicillinase.

Many of the strains were already resistant before penicillin treatment was started.

The epidemiological and clinical significance of these findings has been briefly discussed. The frequency with which penicillin-resistant strains are carried in the anterior nares of ward nurses is thought to be partly responsible for the high proportion of hospital infections with resistant staphylococci.

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The June report of the British Control Commission for Germany says that the Rockefeller Institute has arranged a study tour in Denmark, England, and the U.S.A. for a number of young German medical officers of health, two of whom will probably come from the British Zone. The tour will last two to three months. In the hope that the proposed central narcotic administration for Western Germany may be modelled on British organization, arrangements are being made to send prospective officials to Britain for a 10-day visit to study British methods. No special shortages of medical supplies were reported during the month. Improvement in the supply of penicillin should enable a reserve to be built up again, and it is now sold more cheaply.

HOMOLOGOUS SERUM JAUNDICE

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In 1938 MacNalty drew attention to the fact that jaundice had followed the subcutaneous injection of convalescent measles serum; of 109 recipients 41 developed jaundice. Despite this and similar reports, little interest was aroused until in 1942 Sawyer *et al.* reported 28,585 cases among United States troops following inoculation against yellow fever with vaccine suspended in human serum. Subsequently there were reports of jaundice following the transfusion of human plasma or serum. In 1943 a memorandum was published (*Lancet*, 1943) by Medical Officers of the Ministry of Health reviewing the literature on homologous serum jaundice and reporting that recipients of plasma transfusions had developed jaundice. Spurling, Shone, and Vaughan (1946), in their survey of 1,054 patients given plasma, found that 7.3% developed jaundice, whereas in 891 patients given whole blood there were no cases of jaundice which could be attributed definitely to transfusion. Brightman and Korns (1947) investigated 649 cases in which plasma had been transfused, and found a 4.5% incidence of jaundice.

From these and other reports it was obvious that certain pools of plasma were definitely icterogenic while others were non-icterogenic. It therefore seemed probable that the icterogenic factor was present in the blood of a small percentage of donors, and that the inclusion of such donors' blood in the pools was responsible for their icterogenicity. It was considered likely that by limiting the number of donors contributing to each pool it should be possible to limit the dissemination of the icterogenic agent, and accordingly small-pool plasma was introduced in June, 1949.

This paper reports the results of a survey carried out during the period October, 1945, to March, 1948, in the region served by the Liverpool Regional Blood Transfusion Centre. The main object of the survey was to obtain comparative figures for the incidence of homologous serum jaundice following the transfusion of different blood products. The transfusion materials investigated were:

Large-Pool Plasma.—This consisted of plasma processed at the Medical Research Council Drying Plant at Cambridge or the Army Blood Supply Depot at Bristol before June, 1945, each pool being derived from not fewer than 300 donors; this plasma was Seitz-filtered before drying. In addition to this a small quantity of similar large-pool dried serum, supplied during the war by the Government of the Dominion of Canada and the Canadian Red Cross Society, was used. It was considered that no useful purpose would be served by recording separately cases receiving large-pool plasma and large-pool serum.

Small-Pool Plasma.—Consisting of unfiltered plasma, collected and processed since June, 1945, each pool being derived from not more than 10 donors.

Whole Blood.—Collected and bottled by the standard technique of the National Blood Transfusion Service.

*Working with a grant from the Medical Research Council.

Method of Follow-up

The survey was carried out on the following lines: (1) Names of patients receiving transfusions were reported to the Regional Transfusion Centre by the hospitals. (2) Permission was obtained from the hospitals to abstract from their records information such as the patient's home address, the condition for which the transfusion was given, and other relevant details. (3) After a period of six months from the date of transfusion had elapsed a letter was sent to the patient's home address. This letter was in the form of a general inquiry regarding the health of the patient following his discharge from hospital. A questionary was included with the letter, and the patient was asked to indicate whether he had had various illnesses, including jaundice. On receipt of the completed questionary, those patients whose replies indicated that jaundice had occurred were visited.

This "home visit" was essential for the discovery of cases of homologous serum jaundice, because very few were reported by hospitals or private practitioners. Furthermore, it was necessary to ascertain whether jaundice had occurred in other members of the patient's household, as if this had occurred it was doubtful whether the illness of the recipient could be attributed to transfusion. When full details of the course of the illness had been obtained from the patient, further inquiries were made from the physician who had treated the case, so establishing a comprehensive history and accurate diagnosis.

The "home visit" was omitted in the case of death of the recipient, and a careful check of the case papers and the private practitioner's records was carried out to ensure that homologous serum jaundice had not occurred.

A diagnosis of homologous serum jaundice was made only if each of the following conditions was fulfilled: (1) jaundice occurring one to six months after transfusion; (2) absence of history of contact with cases of infective hepatitis; and (3) absence of other pathological causes of jaundice.

TABLE I.—*Particulars of Patients given Blood, Large-Pool Dried Plasma, and/or Small-Pool Dried Plasma*

	Blood Alone	Large-Pool Plasma	Blood and Large-Pool Plasma	Blood and Small-Pool Plasma	Small-Pool Plasma	Totals
Total No. of patients followed up	4,270	893	666	703	584	7,116
No. of patients untraced	704 (16·4%)	133 (14·8%)	173 (25·9%)	83 (11·8%)	50 (8·5%)	1,143 (16·1%)
No. of patients traced	3,566	760	493	620	534	5,973
No. of deaths within 6 months of transfusion (not with jaundice)	770 (21·6%)	307 (40·4%)	126 (25·5%)	202 (32·6%)	138 (25·8%)	1,543 (25·8%)
No. of surviving patients upon whom incidence of jaundice is based	2,796	453	367	418	396	4,430
No. who reported no history of jaundice within 6 months	2,772 (99·1%)	399 (88·1%)	320 (87·2%)	410 (98·1%)	391 (98·8%)	4,292 (96·9%)
No. with unconfirmed history of jaundice or doubtful aetiology	2 (0·1%)	0 —	1 (0·3%)	1 (0·2%)	0 —	4 (0·1%)
No. who developed jaundice attributed to transfusion within 6 months after transfusion	22 (0·8%)	54 (11·9%)	46 (12·5%)	7 (1·7%)	5 (1·3%)	134 (3·0%)
No. who died of jaundice	0 —	3 (0·7%)	3 (0·8%)	1 (0·2%)	0 —	7 (0·2%)

Overall case mortality rate = 5·22%.

In three of the four cases listed as "doubtful" the history of jaundice was extremely vague, and it was not possible to obtain confirmation of the illness from the patients' private doctors. In the fourth case the patient had been in contact with a case of infective hepatitis.

Of the 1,543 patients who died within six months of transfusion without evidence of jaundice or hepatitis, 1,308 (84.8%) died within one month and 235 (15.2%) within the next five months.

Results of Follow-up

Particulars of the patients followed up are shown in Table I. Letters were sent to 7,116 recipients of transfusion, and 5,973 were traced, of whom 1,543 were reported to have died within six months, leaving 4,430 to be interviewed.

Classifying these according to fluid transfused, 2,796 received whole blood, 453 large-pool plasma, 396 small-pool plasma, 367 blood and large-pool plasma, and 418 blood and small-pool plasma. In all, 134 cases of jaundice were discovered.

The 2,796 recipients of whole blood were given 6,210 bottles, equal to an average of 2.2 bottles per patient. Twenty-two cases of homologous serum jaundice occurred following the use of these 6,210 bottles of blood: if each case of jaundice received only one bottle of icterogenic blood, and assuming that each donor gave only one bottle of blood, then at least 0.35% of the donors were carrying an icterogenic agent in their blood stream with no symptoms indicative of disease. It is unlikely that all recipients were susceptible, so that the rate is possibly higher than this.

Among those who received large-pool plasma and blood and large-pool plasma 100 cases of homologous serum jaundice occurred. The batches of plasma used in six of these cases were also found to be icterogenic when used in other areas. Seventy-one of the cases followed the use of 25 batches—for example, Batch No. C307 was involved in seven cases. Each of the remaining 23 cases was associated with a different batch of plasma.

Similarly, among those receiving small-pool plasma and blood and small-pool plasma the plasma used in six of the 12 cases was drawn from 13 different batches. The remaining six cases each followed the use of a different batch. These batches were not associated with jaundice in any other recipients.

It is impossible to give an attack rate for any particular batch of icterogenic plasma in this series, but it was found, for example, that Batch No. C307 was given to 15 patients without complication, although this batch was followed by jaundice in seven other patients. The total number of recipients of this batch, which was widely distributed in other areas, is not known.

Fatal Cases.—There were seven deaths from homologous serum jaundice in the series—namely, three in the large-pool plasma group, three in the blood and large-pool plasma group, and one in the blood and small-pool plasma group. There were no fatal cases in the groups which received small-pool plasma or whole blood (see Table II).

TABLE II.—*Fatal Cases*

Illness	Age	Sex	Incubation Period	Transfusion Fluid
Incomplete abortion ..	36	F	12 weeks	Blood and small-pool plasma
Post-partum haemorrhage	28	F	16 ,,	Blood and large-pool plasma
Arthrodesis of hip ..	55	M	6 ,,	,, ,, ,, ,,
Ruptured spleen	40	M	6 ,,	,, ,, ,, ,,
Multiple injuries and shock	73	M	9 ,,	Large-pool plasma
Prostatectomy	67	M	13 ,,	,, ,,
Partial gastrectomy ..	65	M	6 ,,	,, ,,

Incubation Period.—The incubation period of the illness varied considerably in the cases investigated, but unless the jaundice occurred between one and six months after transfusion it was not classified as homologous serum jaundice. In fact, no cases of jaundice occurred within one month of the transfusion. In the majority of cases the jaundice occurred 8 to 16 weeks after transfusion (see Chart).

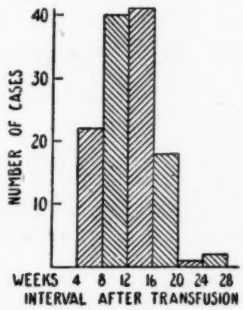

Chart showing incubation period. Ten cases are omitted because the incubation period could not be accurately determined.

Nature of the Illness.—Eight of the cases (6%) were very mild, with an illness lasting less than one week, and three of these were indisposed for two to three days only. On the other hand, two cases terminated fatally within three days of the onset of symptoms. Twenty-one cases (15.7%) were severe, with an illness which lasted six weeks or more, while the remaining 98 cases (73.7%) were ill for one month or less and their symptoms were not severe. The average duration of illness was 30.5 days, with extremes of two and 112 days. The incidence of the various symptoms and signs is shown in Table III.

TABLE III.—*Symptoms and Signs*

Symptoms and Signs	No. of Cases
Jaundice	134 (100%)
Nausea, vomiting, and anorexia	60 (44·8%)
Lassitude	35 (26·1%)
Joint pains	33 (24·6%)
Skin rash	21 (15·7%)
Epigastric pain	14 (10·4%)

Age Incidence.—The age incidence is set out in Table IV; the upper and lower limits were 73 years and 9 years respectively.

TABLE IV.—*Age Incidence*

Age Group	No. of Patients Transfused		No. of Cases of Jaundice	
	Blood Alone	Plasma and Plasma and Blood	Blood Alone	Plasma and Plasma and Blood
0–10 ..	87	127	—	1 (0·8%)
11–20 ..	136	104	2 (1·4%)	6 (5·7%)
21–30 ..	655	294	6 (0·9%)	20 (6·8%)
31–40 ..	758	339	7 (0·9%)	24 (7·1%)
41–50 ..	480	254	2 (0·4%)	23 (9·1%)
51–60 ..	294	204	2 (0·6%)	19 (9·3%)
61–70 ..	267	211	2 (0·7%)	17 (8·1%)
71–80 ..	112	88	1 (0·8%)	2 (2·2%)
81–90 ..	7	13	—	—
Totals ..	2,796	1,634	22 (0·8%)	112 (6·1%)

The illness which necessitated transfusion therapy was taken into account in all cases, but nothing significant was noted. Similarly, the cases were more or less equally distributed between the sexes, 71 (53%) being female and 63 (47%) male.

Discussion

In the present investigation the incidence of homologous serum jaundice (11.9%) found among the recipients of large-pool plasma is considerably higher than that reported by other workers. Of the 54 cases, three were fatal, whereas Spurling and others reported 77 cases, none of which was fatal.

In those patients who received small-pool plasma, on the other hand, the incidence of homologous serum jaundice was significantly lower, amounting to only 1.3%. The considerable reduction in the incidence of this complication of plasma transfusion seems to justify the decision made in 1945 to produce only small-pool plasma.

Of the recipients of whole blood 22 developed jaundice—i.e., 0.8% of the cases—whereas among 891 recipients investigated by Spurling and others six cases of jaundice (0.7%) were reported, but these were listed as "doubtful if due to transfusion."

Inquiry failed to reveal any increase in the incidence of infective hepatitis during the period under review in the North-West Region, the population of which is 3,250,000. In another part of England the attack rate per 1,000 per annum was 0.06 in 1945, 0.07 in 1946, and 0.04 in 1947 in a population of 2,600,000 (McFarlan—personal communication).

In the production of small-pool plasma a record of the donors who contributed to each pool was available, and a follow-up of these donors was carried out so far as was possible, but in only one out of the 63 donors traced was there a history of jaundice. In this case jaundice occurred three months after blood donation. No information such as history of contact with infective hepatitis or of inoculation was given. The donors whose bloods were involved in homologous serum jaundice in the whole-blood series were also followed up, but with negative results.

Summary

In the follow-up of 4,430 patients who had received transfusion therapy 134 (3%) cases of jaundice were discovered, of which seven (0.2%) terminated fatally.

Large-pool plasma and combined large-pool plasma and blood transfusions were responsible for 100 (74.6%) of the cases, six of which were fatal.

The incidence rates of homologous serum jaundice for small-pool plasma (1.3%) and for whole blood (0.8%) are not significantly different (difference/S.E. of difference = 1, approx.), but these rates differ very considerably from that of large-pool plasma (11.9%).

The findings suggest that at least 0.35% of donors are probably carriers of the icterogenic virus.

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One of the German casualties of the war was the *Archiv für Schiffs- und Tropenhygiene*, and for over four years the Germans have been without a national journal devoted to tropical medicine. This gap has now been filled by the publication of the *Zeitschrift für Tropenmedizin und Parasitologie*, which is edited by workers at the Bernhard Nocht-Institut für Schiffs- und Tropenkrankheiten, Hamburg, and published by Georg Thieme, of Stuttgart. In their prefatory note the editors point out that, while opportunities for German workers in the Tropics are now almost non-existent, many problems concerning tropical medicine can be investigated in the laboratory at home, and that as a result of the war many cases of tropical disease in Germany make ample material available for clinical investigation. Subscription to the new journal is approximately £4 per annum. Dutch investigators also suffered a setback when publication of the *Geneeskundig Tijdschrift voor Nederlandsch Indië* was stopped by the Japanese in March, 1942, after having appeared without interruption since 1852. This journal was replaced in 1946 by the *Medisch Maandblad*. Both these journals have the disadvantage, so far as English readers are concerned, of being almost entirely in Dutch. To overcome this difficulty the Dutch have now commenced publication of an English-language quarterly journal of tropical medicine and hygiene, *Documenta Neerlandica et Indonesica de Morbis Tropicis*, with an editorial board representative both of the Netherlands and its overseas territories. Subscription to this journal is £1 2s. 6d. per annum, and it is published at Rivierenlaan 268, Amsterdam Z.

ISO-IMMUNIZATION BY BLOOD-GROUP FACTORS A AND B IN MAN

BY

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Much has been written about the possibility of the blood-group factors A and B acting in the same way as the Rh factor in the pathogenesis of haemolytic disease of the newborn. Jonsson (1936) gave the first immunological evidence, of a statistical nature, that heterospecific blood-group pregnancy (where the O or B mother bears a foetus of group A or AB) was accompanied by a rise of the anti-A haemolysin. Smith (1945) demonstrated that the anti-A or anti-B agglutinin titre rose only in the cases in which the heterospecific foetus was a secretor. The heterospecific pregnancy is then capable of inducing an immune response, but there are very few heterospecific foetuses that demonstrate haemolytic disease. In consequence, there must be some protective mechanism, several of which were reviewed by Tovey (1945).

There are, however, certain facts which focus the attention on the antibody itself. In 1946 we found in the blood of pregnant women who had previously been delivered of stillborn babies anti-A agglutinins reacting far more strongly at 37° than at 4° C. (Millet and Hubinont, 1946a ; Hubinont and Millet, 1946). Bruynoghe (1947) found an anti-B agglutinin of the same type in a case of haemolytic disease of the newborn. Since then we have met with several similar cases in which the clinical course was somewhat different from the classical haemolytic disease of the newborn. In all cases the foetus died *in utero* a few days before delivery or during labour.

Many authors—the first of them being Levine, Katzin, and Burnham (1940)—have emphasized that anti-Rh agglutinins react more strongly at 37° than at 4° C. Inversely, it is very well known that natural anti-A or anti-B agglutinins possess a thermal optimum at 4° C.

We verified that several normal agglutinins of rabbit serum (Millet and Hubinont, 1946b ; Hubinont, 1948a) and guinea-pig serum (Hubinont, 1947) showed, through immunization, the same change of thermal optimum that we found in our patients. Further investigations on the rabbit showed that hyperimmunization with sheep erythrocytes was often followed by the production of a blocking antibody, giving a prozone phenomenon in quantitative agglutination tests (Hubinont, 1948b).

We recently had the opportunity of studying the immune-response of a group B individual who was transfused by mistake with A_1 blood and eventually recovered: 75 ml. of whole blood had been injected before alarming symptoms appeared.

The serum was tested at regular intervals with A_1 and A_2 cells collected from the same donors. The tests were performed by the usual technique in tubes, using 0.9% saline as diluent, each test being performed simultaneously at 4° and 37° C. The results are shown in the Table.

On the day of transfusion both A_1 and A_2 cells were agglutinated with the same titre and thermal optimum. On the fourth day there was a small increase in titre, noticeably higher for A_1 than for A_2 cells. On the eighth day the thermal optimum for A_1 agglutination turned to 37° C. Finally, on the 30th day the agglutination was stronger at

37° C. for both A_1 and A_2 cells. Further, there was a prozone phenomenon in the test for A_1 agglutination at 4° C. It was shown by a blocking test (Race, 1944 ; Wiener, 1944) that this prozone was due to the presence of an anti-A blocking antibody.

Time of Test	Cells	Temp.	Serum Dilutions 1/1	1/2¹	1/2²	1/2³	1/2⁴	1/2⁵	1/2⁶	1/2⁷	1/2⁸	1/2⁹	T
Day of transfusion	A_1	37° C.	3½	3½	3½	2½	2	1	++	++	—	—	—
		4° C.	3½	3½	3½	2½	2	1	++	++	—	—	—
	A_2	37° C.	++	++	w	—	—	—	—	—	—	—	—
		4° C.	3	3	2	2	1	++	++	—	—	—	—
4th day	A_1	37° C.	2	2	1	+	w	—	—	—	—	—	—
		4° C.	4	4	4	3	3	2	1	++	+	—	—
	A_2	37° C.	++	++	(+)	?	?	—	—	—	—	—	—
		4° C.	4	3½	3	3	1½	+	(+)	w	?	—	—
8th day	A_1	37° C.	4	4	4	4	4	3	2	1	½	++	—
		4° C.	4	4	4	4	3	2	2½	1½	++	(+)	—
	A_2	37° C.	4	4	3½	3½	3	2½	1	½	++	(+)	—
		4° C.	4	4	4	3½	3½	3	3	2	½	++	—
30th day	A_1	37° C.	2½	4	3½	3½	3½	3½	3	2½	2	2	—
		4° C.	++	(+)	++	++	2	3½	3½	2	1	++	—
	A_2	37° C.	2	2	3	2	3½	3	2½	2	2	1½	—
		4° C.	3½	3½	2½	3	3	3	2½	2	1	++	—

Scores for agglutination are given in arabic signs (for visual agglutination) and the signs usually employed for microscopical agglutination in Rh work (M.R.C. Memorandum, 1943).

Unfortunately the patient could not be followed up, and we are not aware of his actual agglutination pattern for A_1 and A_2 cells. Nevertheless, his immune response to an incompatible transfusion confirms our observation of ABO iso-immunization in pregnant women and of experimental hetero-immunization in rabbits.

Upon immunization with an antigen corresponding to a natural agglutinin present in the animal's serum (anti-A or anti-B in man, anti-sheep in rabbits), the first noticeable change would be a slight rise in titre, followed quickly by an inversion of the thermal optimum in quantitative agglutination tests. A further step would be the apparition of a prozone corresponding to the production of "blocking antibodies."

The *in-vitro* differences in the behaviour of "natural" cold anti-A and anti-B agglutinins and the "immune" warm anti-A and anti-B antibodies are probably dependent on their chemical structure, which would account for their harmfulness to the foetus. It is a significant fact that we found these warm agglutinins in the only instances quoted above with their particular clinical course, and that they were not found in uneventful heterospecific blood-group pregnancies.

Summary

A case of immune response to an incompatible blood-group transfusion is described. There is a definite difference *in vitro* between natural and immune anti-A agglutinins.

The same difference is found in maternal iso-immunization, the particular form of haemolytic disease following A and B sensitization being the death of the foetus *in utero*, either during the last days of pregnancy or at the time of delivery.

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DIAGNOSIS AND TREATMENT OF CUTANEOUS ANTHRAX

BY

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Anthrax—a rare disease in this country—has many interesting and unusual facets. Probably first recorded by Virgil, it became prominent initially in Britain about the middle of the last century coincidentally with the importation of alpaca and mohair to Bradford. It was first notifiable so far as factories and workshops were concerned in 1896, and activity was rapidly directed towards its prevention in view of the high proportion of fatalities among affected workers —then some 20 to 30%. Local precautions in the form of protective clothing, the posting of information regarding the disease, washing facilities, and exhaust ventilation for certain processes were advocated by the Anthrax Investigation Board set up in Bradford by the Chamber of Commerce. Despite these the incidence remained high, though the dread and fatal form of pulmonary infection showed a rapid decline between 1881, when Mr. John Spear made his investigations, and 1905, when Dr. T. M. Legge gave the classical Milroy Lectures on industrial anthrax.

A further Anthrax Investigation Committee set up in 1913 advocated, in 1918, a process for wool and hair disinfection. Following up the committee's suggestions, Parliament passed the Anthrax Prevention Act in 1919, and by 1921 an experimental disinfecting station had been set up in Love Lane, Liverpool, to carry out the "Duckering process"—named after the secretary of the above committee—for wool and hair disinfection, and in succeeding years this process has proved its efficacy. Mention should be made of the excellent bacteriological investigations carried out for both the board and the committee by the late Dr. F. W. Eurich, professor of forensic medicine at the University of Leeds.

From 1890 to 1920 an increase in the incidence of anthrax was also noticed in the cattle of Great Britain, though the numbers were never comparable to those encountered in Russia, Siberia, China, and parts of India. Knowledge about the means of spread of the disease and the life history of the organism enabled measures to be taken which may be briefly summarized under the headings of—notification, isolation, and destruction of the sick animal or carcass, disinfection of the surroundings, and inoculation of other animals. These not only rapidly controlled the disease among cattle but also diminished the incidence among butchers, veterinarians, shepherds, and others associating with animals, the true index of which was never known, since only cases occurring in certain trades were then notifiable. This anomaly of notification was widely commented upon in coroners' courts, medical journals, and Parliament at the time.

In the four or five years following 1915 the incidence of anthrax increased both here and in America, the source being shaving-brushes made from infected hair. This source was soon recognized as being especially dangerous, since it was not confined to any particular trade or industry, claiming among its victims a professor of law and a

Congregational minister, to name but two, and precautions were rapidly taken—in particular an Order made under the Act of 1919 banning the importation into Britain of shaving-brushes of Japanese origin. Sporadic cases from this source have been reported up to 1939—some from brushes bought years previously, in which the spores had lain dormant until the unlucky coincidence of shaving-cut and spore ignited the powder of disease.

The disease contracted from wool and hair and that in animals are thus largely controllable, but there still remains a further common source of infection—namely, imported hides and skins. This source gives rise to cases not only in tanneries but also in dock workers, carters, and warehousemen, as well as very occasionally in persons coming in contact with leather. Methods aimed at killing the hardy spore in the hides tend to damage the material, and though suitable disinfecting processes have been claimed by Seymour-Jones, of Wrexham (and advocated by Ponder), and by others in Germany, they have not been adopted. Cases from this source arise from time to time, and the following is a report of eight such cases occurring in two tanneries in Leeds and district in a period of fourteen months.

Occupation and Source of Infection

All eight cases were of the cutaneous type of infection, and all occurred in men doing essentially the same tasks at two different tanneries (named for convenience "A" and "B") in widely separated areas. Tannery "A" deals mainly with goat-skins coming from various sources as indicated in Table I, but principally from East and West Africa. All six men from this tannery were employed opening the bales of skins, carrying the skins up to a sorting-shed, sorting them, and then sending them down a chute to the lime-yard when required. As one man after another fell victim other men took their place, and eventually they too became patients. Of the seven different men undertaking these tasks during the past fourteen months six have contracted anthrax. The previously reported cases occurring at this tannery were two in 1936 and two in 1946. Certain alterations have now been carried out in the hope of reducing the risk.

Tannery "B" deals with cowhides chiefly from East and West Africa, though occasionally from South America and India. All are dry hides, as opposed to the wet salted variety which rarely give rise to infection. The duties of the men at this tannery are precisely the same as those at "A"—but owing to the demand for goods and the shortage of raw material there is very little storage of hides at present, and they are almost immediately taken to the water- and lime-vats on unbaling, and there is no chute system. During the eight-months period in which cases occurred there were some 12 to 15 men working in this part of the tannery. There had been no previous cases.

At both tanneries the full regulations as laid down in various Acts are carried out, the men wearing protective clothing, and washing facilities and changing-rooms being provided. In the opinion of the authorities at these tanneries it is the increased demand for raw materials which has given rise to the present outbreak, the materials being collected from various remote regions in Africa where there is little or no control over the source of the hide or skin. No cases have ever occurred at either tannery in the processes carried out beyond the lime-vats.

Occurrence of Infection. Contact Cases

The necessity for a local skin abrasion together with the presence of the organism before the appearance of a malignant pustule has long been known, and is borne out by these cases, in all of which there was good cause for a local abrasion such as collar-chafing or shaving-cuts. Even in Case 4, in which the lesion was on the leg, there were also numerous flea-bites. It is interesting to speculate in this connexion whether a break in the lung "lining surface" is not also necessary before the development of pulmonary anthrax. Spore-laden dust was plentiful at tannery "A" and yet no pulmonary cases have occurred to date. Also the rapid decline in incidence of pulmonary anthrax from 1880 onwards parallels the improvement in general public health and the decline of tuberculosis in particular.

All cases presented the classical malignant pustule, and in all the diagnosis had been made by the patient or a fellow workman—from their knowledge of the disease obtained by experience or from a poster hung in the factory—and never by a physician. In some cases delay in admission was actually caused by the physician.

Man-to-man infection is surprisingly rare. There are recorded cases in the literature—Hodgson (1937) records two—but their number is small, and this is surprising in view of two points which can be seen in Tables I and III—namely, the length of time during which the patient may be in contact with his family, often in a small house, and the fact that his normal healthy skin may give a positive growth of organisms, showing the widespread nature of their distribution. The intact skin must in many cases be a barrier of unusual strength in preventing the appearance of contact infection.

TABLE I.—*Summary of Cases*

Case	Age	Tannery	Source of Hides	Site of Lesion	Duration	Stay in Hospital	Date of Admission	Constitutional Symptoms on Admission	Smear	Culture	Animal Inoculation	Contacts
1	50	A	Indian and E. African goat-skins	Below and behind right ear	26 hrs.	24 days	27/11/47	Nil	Pos.	Pos.	Pos.	4
2	48	A	E. African goat-skins	Left temple	4 days	17 ,,	22/12/47	,,	,,	,,	,,	1
3	42	A	,, ,, ,,	Right side of neck	3 ,,	16 ,,	16/2/48	,,	,,	,,	,,	7
4	49	A	E. and W. African goat-skins	Posterior right calf	20 hrs.	13 ,,	21/2/48	Severe	,,	,,	,,	7
5	29	A	,, ,, ,,	Right cheek	4 days	13 ,,	22/2/48	Nil	?Pos.	Neg.	Neg.	2
6	53	A	,, ,, ,,	Posterior right neck	6 ,,	33 ,,	20/8/48	,,	Pos.	Pos.	Pos.	1
7	30	B	E. and W. African cowhides with some S. American and Indian	Left cheek	3 ,,	17 ,,	29/5/48	,,	,,	,,	,,	2
8	29	B	S. African and Nigerian cowhides	Below and behind right ear	3 ,,	19 ,,	24/12/48	,,	,,	,,	,,	4

Diagnosis

This is made on the following three salient points.

1. *Appearance of Lesion.*—In all eight cases this was typical—a black, necrotic centre, a ring, partial or complete, of pearly translucent vesicles, the whole sitting on a red base on a hillock of widespread oedema. Certain other features aid the physician. The absence of pain with such a degree of oedema is noticeable. Practically the only local symptom encountered in this series was slight itching.

Earlier stages than this in the development of the lesions are described, the commonest being the large vesicle under which the black eschar forms, but these were not seen by us even in the patient who presented within 26 hours of the onset of disease. Constitutional symptoms and signs were not common. Only Case 4 presented with pyrexia, though Cases 3, 6, and 8 had pyrexia on the second or third day of treatment, with associated headache, malaise, and often pains in the bones. In Case 6 this may have been of other causation (see below).

2. *Occupation of Patient.*—At present this is a reasonably straightforward clue, anthrax occurring in those industries where exposure to infection is well known. A survey of the literature has shown that the disease may appear under most unlikely circumstances. For example, it may occur in carpet-layers, paper-hangers (from wall plaster), menders of sacks (which have carried bones, horns, or hooves), and carriers of potatoes (from soil), and from mink farms, elephant tusks, elephants at the London Zoo, etc. A physician may be forgiven for not suspecting the condition in patients in occupations such as these, but in persons connected with animals or animal products (especially imported ones) presenting with a localized skin lesion, or occasionally multiple lesions, anthrax should be a first consideration.

3. *Bacteriological Diagnosis and Investigations.*—These are the final proof, and were obtained in all our cases except Case 5, in which the first two criteria were adequately fulfilled—justifying treatment for anthrax. The following investigations were carried out in this series.

Bacteriological Examination

As soon as a case was suspected of being due to *Bacillus anthracis*, material from the local lesion was taken for investigation. The most practicable way of taking this material was found to be with a Pasteur pipette, plunging the point into the centre of a vesicle, or vesicles if confluent, and withdrawing the fluid. If there were no obvious vesicles, or they had burst, then material was aspirated from beneath the edge of the eschar. The fluid obtained was clear, yellow, or sanious in nature, there being no evidence of pus macroscopically.

As a routine this material was cultured aerobically on heated and fresh blood agar, and two thick films were made, stained with Gram and Leishman respectively. On examination of the Gram film a long time was often spent before coming across one, two, or perhaps a small chain of bacilli—this being especially true in five of the seven positive cases. In the other two the vesicular fluid was heavily infected with the organism. In no case was there any marked polymorphonuclear leucocytic response. In the seven positive cases the appearance of the bacillus was morphologically typical of *B. anthracis*—a large, straight, capsulated, Gram-positive bacillus with parallel sides, clean-cut square ends, with a tendency to chain formation. As confirmed by others, there was no evidence of spore formation in the human tissue fluids.

The growth after 18 to 24 hours on the solid media invariably showed an almost pure culture of *B. anthracis*, with occasional colonies of *Staphylococcus albus* and diphtheroids. There was no evidence in any case of invasion by other pyogenic organisms. The colonies at 24 hours' growth had the typical reticulated surface with irregular wavy edges (so-called barrister's wig), producing proteolysis on the heated blood-agar medium and no haemolysis on the medium containing the fresh blood.

These colonies were subcultured, and after the organism had been isolated in pure culture the following investigations were carried out.

Morphology.—Routine films from the 24-hour culture showed the typical rod-shaped appearance of the organism in heavy interlacing chains, capsulated, and associated with the production of numerous spores. These were mainly central or subterminal, but there were many spores also lying free. The characteristic morphology was retained on repeated subculture.

Motility.—This was determined by growing the organism in a semi-solid nutrient-agar medium in a 1-in. (2.5-cm.) diameter boiling-tube. A small-bore glass tube was inserted into the boiling-tube, the *B. anthracis* being inoculated on to the surface of the agar in the small tube. The organism, being non-motile, remained localized on or just below the surface of this agar. If the organism had been an anthracoid, then owing to its motility growth would have proceeded down the small tube and eventually infiltrated the larger volume of agar outside. In all the seven strains investigated the organism was non-motile.

Proteolytic Activity.—Gelatin prepared in large boiling-tubes was inoculated as a stab culture at 24° C. The lytic effect in gelatin is a slow but definite effect. In two cases only did the organism produce the truly characteristic inverted fir-tree phenomenon. The other five strains seemed to produce little attempt at canalicular liquefaction, there being just a central core of proteolysis.

Effect of Antibiotics.—All the strains were tested for their sensitivity to penicillin and streptomycin. The usual punch-hole plate method was adopted. Table II shows the degree of inhibition compared with that of the Standard Oxford *Staph. aureus*. Thus in all cases the strain was sensitive to both penicillin and streptomycin in fairly low concentrations. It is interesting to observe that on the whole the strains showed greater inhibition with streptomycin than with penicillin, using equivalent concentrations of streptomycin per ml. No production of strains resistant to these drugs was noted, as the organism was never recovered from the lesion after the patient was placed on intensive treatment. The strains on an average were sensitive to 10 units of penicillin per ml. and to 5 to 10 units of streptomycin per ml.

TABLE II.—*Sensitivity to Antibiotics: Animal Pathogenicity*

Case No.	Strain	Sensitivity Compared with Oxford *Staph. aureus*		Death of Mouse after Inoculation
		Penicillin	Streptomycin	
1	I	25% less	Equivalent	34 hours
2	II	50% ,,	10% less	36 ,,
3	III	10% ,,	80% ,,	36 ,,
4	IV	20% ,,	10% ,,	30 ,,
6	V	25% ,,	5% ,,	20 ,,
7	VI	20% ,,	10% ,,	35 ,,
8	VII	Equal	75% ,,	30 ,,

Animal Pathogenicity.—In the seven cases in which the organism was isolated the mouse was utilized for virulence tests. A volume of 1 ml. of a 24-hour "oxopeptone" broth culture was injected subcutaneously into the right half of the anterior abdominal wall. The animals were isolated in glass containers, the carcass, food, faeces, etc., being autoclaved after necropsy. Death occurred in all cases within 36 hours, as shown in Table II. At necropsy the local lesion was haemorrhagic, hyperaemic, and oedematous, the spleen was congested and enlarged, and on microscopical examination the oedema fluid, splenic pulp, and heart blood were found to contain enormous numbers of Gram-positive bacilli, yielding pure heavy growths of *B. anthracis* on culture.

In addition to the above investigations on individual strains, in each case a series of swabs were taken from the hair or skin of the patients in order to ascertain the presence or otherwise of *B. anthracis*. Table III summarizes the

results of these investigations, carried out before the third day of treatment (usually on the first day). Similar investigations made towards the end of the stay in hospital were negative, as were cultures made from materials taken from beneath the eschar after complete therapy.

TABLE III.—*Skin Cultures*

Case No.	2 in. Above Lesion	2 in. Below Lesion	Hair of Scalp	Right Palm	Left Palm	Right Groin	Left Groin
1	Neg.	Pos.	Pos.	Neg.	Neg.	Neg.	Neg.
2	"	Pos. A	Neg.	"	"	"	"
3	"	Neg.	"	"	"	"	"
4	"	"	"	"	"	"	"
5	"	"	"	"	"	"	"
6	"	"	"	"	"	"	"
7	"	"	"	Pos.	"	"	"
8	"	"	"	"	"	"	"

Neg. indicates only normal flora grown. Pos. indicates *B. anthracis* cultured. Pos. A indicates anthracoids cultured.

Treatment

In no case was surgery contemplated. Excision and incision, especially the murderous crucial incision which was once performed, play no part in the modern treatment of anthrax, and are probably harmful, breaking down natural barriers. A study of the literature has revealed that excision performed very early was possibly beneficial, but incision was almost invariably followed by death, and thus was much worse than no treatment at all. In this series the local lesion was covered with a dry sterile dressing and left alone after the necessary bacteriological examinations. The part was immobilized as far as possible: if on the head and neck the patient was nursed flat with the head between sandbags; if on a limb, as in Case 4, the limb was splinted. The following specific treatment was

TABLE IV.—*Treatment*

Case	N.A.B.	Serum	Penicillin (units)	Result
1	1·5 g. over 10 days	145 ml. in 4 days	650,000	Cure
2	1·05 g. in 6 days	90 ml. in 5 days	2,265,000	"
3	1·2 g. over 5 days	160 ml. in 5 days	1,344,000	"
4	1·2 g. over 8 days	240 ml. in 5 days	3,520,000	"
5	1·2 g. over 5 days	80 ml. in 2 days	2,048,000	"
6	1·2 g. over 6 days	320 ml. in 4 days	5,400,000	"
7	1·8 g. over 13 days	80 ml. in 2 days	2,800,000	"
8	1·2 g. over 6 days	420 ml. in 6 days	6,018,000	"

carried out (Table IV), since the literature concerning patients treated successfully with penicillin alone had not been studied when the first case was admitted.

Neoarsphenamine.—This drug was given in two or three doses of 0.45 to 0.6 g. intravenously at five- to seven-day intervals. Doses such as these given once or twice at one- to three-day intervals have been used successfully without any other therapy (Becker, 1912a, 1912b; Pijper, 1926).

Anti-Anthrax Serum.—Until recently this has been the mainstay of treatment. Advocated by Sclavo in Italy, by Marchoux in France, and by Legge (1905) in Britain, it soon became widely used—at first in combination with surgical treatment, and later alone, with definite success. Dosage advocated differed—from 40 to 80 ml. by early workers (Legge, 1905; Lockwood and Andrewes, 1905; Bowlby and Andrewes, 1905) to 600 ml. and upwards (Hodgson, 1941; Gold, 1942). In the above series the average dosage was 190 ml. in some seven injections over four days—the total varying with the need and response of the patient. Usually between 60 and 100 ml. was given intravenously on the first day of treatment. No severe reactions were encountered during the time of serum administration, but all cases developed urticaria and pruritus on the eighth day after the start of serum therapy. This was readily controlled by the use of calamine lotion containing 1% phenol locally and "anthisan" internally, 100 mg. three times a day with meals. The serum used, apart from the first case, was that marked "War Agricultural Committee," contained in rubber-capped 500-ml. bottles. Case 1 had the product manufactured by Mulford's, and later some 90 ml. of Lister's antiserum.

Penicillin.—Several reports are now in the literature of cases of cutaneous anthrax treated successfully with penicillin alone (Murphy *et al.*, 1944; Ellingson *et al.*, 1946; Griffin *et al.*, 1948). The suggested dose increases as the years go by, starting with a total dose of 200,000 to 400,000 units advocated by Murphy *et al.*, to 5,000,000 units advocated by Griffin *et al.* The average dose used in our series was about 3,000,000 units, given usually as 64,000 units three-hourly, though occasionally as 250,000 units twice daily.

Sulphonamides.—Sulphonamides were used not as specific therapy, though claims have been made for their curative powers in anthrax by Gold (1942), but in an attempt to remove the secondary invading organisms in the lesion—usually *Staph. aureus*. The dosage was small, a total of 15 g. over 10 days being the average. In Case 4 secondary infection with a purulent discharge was very troublesome, and the patient attended as an out-patient for local and general (penicillin) therapy for some two months after the cure of the anthrax.

Case 6 presented an interesting therapeutic problem in that he had latent seropositive syphilis in addition to anthrax. On the fourth day of treatment with serum, neoarsphenamine, and penicillin, he had a pyrexia of some 101° F. (38.3° C.) lasting for eight hours; since this occurred about eight hours after the last injection of serum, the possibility of a Jarisch-Herxheimer reaction was considered. Luckily there was no focal flare-up of the syphilis—at least, it was not in evidence. A study of the literature has not revealed a similar case.

All cases have been visited since discharge from hospital. All possess a small scar which is barely noticeable. All are well, and so far none has contracted any further lesion. Second attacks are uncommon, but do occur (Inda, 1921) and are said to be mild. The two men now doing the dangerous work at tannery "A" are both discharged cases, but it is hoped that the alterations carried out at this tannery have reduced the risk of infection. A third man from tannery "A" has returned to work, but in a job connected with the further processing of the leather and not in the lime-yard. The remaining three have obtained other employment. Both men from tannery "B" have returned to work in their original occupation.

Summary

A brief survey of the sources of anthrax shows control to be applicable and useful in all but hides and skins, and a report is given of eight cases occurring in Leeds and district over a period of 14 months in persons connected with these raw materials.

The salient points concerned in the diagnosis are given, together with the details of the isolation and identification of the organism in seven cases by direct films, culture, biochemical activity, and animal inoculation.

The effect of penicillin and streptomycin on the organism is discussed, and the routine investigation of skin culture before and after treatment is cited.

Methods of treatment past and present are briefly given, and the conclusion is reached that, for all practical purposes, penicillin is probably the most desirable method to-day—from the point of view of effectiveness, time of hospital stay, expense, and unpleasant side-actions.

We wish to express our thanks to Dr. J. T. Ingram and Professor J. W. McLeod for their kind permission to publish these cases, and for their help and advice in the writing of the article; also to Miss J. Cuckston for her invaluable technical assistance.

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ACUTE PERICARDITIS SIMULATING CARDIAC INFARCTION

BY

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Simulation of cardiac infarction by acute pericarditis is well recognized by cardiologists, though references are not numerous (Barnes and Burchell, 1942; Wolff, 1944). Pericarditis in such cases is of unknown aetiology, since an obvious cause would leave no doubt about the diagnosis. It forms a subgroup of the type mentioned by East and Bain (1948), in which "cause and association are quite obscure," and is termed by Peel (1947) "primary or idiopathic," by Dry (1943) "non-specific . . . from which recovery may be complete," and by Andrews *et al.* (1948) "acute idiopathic." The infrequency of specific references seems to justify a report of only two cases. The association of one with a general arterial disease suggests a possible mechanism.

Case 1

A man aged 63 was admitted to the Royal Sussex County Hospital on July 23, 1948, and was diagnosed clinically as a case of temporal arteritis. Biopsy confirmed the diagnosis and relieved a severe headache: the histological report was, "The adventitia is infiltrated with round cells, among which are a few eosinophils and giant cells. There are areas of necrosis in the media. The appearances are typical of temporal arteritis." Though the condition was regarded as still active, with persistent fever, a predominantly polymorph leucocytosis of 11,800, and an erythrocyte sedimentation rate of 31 mm. in the first hour (Wintrobe corrected, normal 0–10), discharge was necessary after a fortnight.

Headaches returned, however, and he was awaiting readmission, when in the early hours of Sept. 21 he was suddenly attacked by a pain under the left costal margin which spread to the lower substernal area. He was admitted 16 hours later, with evident severe substernal pain but negative clinical findings except for fever of 100° F. (37.8° C.) and what was regarded as triple heart rhythm. During the next 24 hours his temperature fell to normal and the pain disappeared, but a pericardial friction rub developed. An electrocardiogram showed changes indicating acute pericarditis, with elevation and deformity of the R–T interval in all leads. This returned practically to normal a fortnight later; no evidence of cardiac infarction was present. He was then discharged, afebrile, but with a raised sedimentation rate, which persisted until he was last seen in February, 1949, when he complained of pains in the occiput, sterno-mastoid, thigh, and deltoid muscles. The heart appeared normal clinically and by electrocardiography and cardioscopy.

Case 2

A man aged 37 was seen on Jan. 19, 1949. Following moderate exposure and mild malaise, and after a heavy meal, he developed epigastric pain while driving his car. This grew more severe and paroxysmal, extending from the xiphisternum upwards to the suprasternal notch, passing outwards to the pectoral regions and posteriorly to the interscapular region at the level of the sixth dorsal vertebra. Although no abnormal clinical signs of any kind were found, repeated injections of "omnopon" and pethidine were necessary.

By the next morning the patient felt practically recovered, but during this second day fever of 101° F. (38.3° C.) developed, and a loud but painless pericardial friction rub became audible. An electrocardiogram showed the changes of acute pericarditis, with elevation and deformity of the R–T interval in the limb leads and chest leads CR1 to CR7, maximal in II and CR3. Friction disappeared in 24 hours and fever in 48 hours. After a fortnight the heart was clinically and cardioscopically normal, but there was still slight elevation of the R–T interval, maximal in II and CR4. After a further seven weeks, when the patient had been working for a month, slight elevation of R–T in CR4 alone remained.

Comment

Both cases were at some stage, and with justification, diagnosed clinically as cardiac infarction. Apart from differential diagnosis, the general question of their mechanism may be raised. As will be observed from the earlier references, none has been suggested. It is also noted by Wolff (1944) that the prognosis is good, as is implicit in the terms "non-specific," "obscure," or "idiopathic" used by other authorities, since fatalities and necropsies would be likely to lead to some conclusion regarding their cause. A bacterial origin seems unlikely, since duration is brief and sequelae are rare. The cases cannot be regarded as "a chief manifestation of an infective process" (Lewis, 1946), such as acute rheumatism (Evans, 1948).

Another possibility arises, however, when the group simulating cardiac infarction is considered. The most likely simulator of a vascular lesion is another vascular lesion. In Case 1 there is evidence of activity of temporal or giant-cell arteritis, now recognized as a generalized process (Cooke *et al.*, 1946). The possibility has been suggested that this may affect the coronary vessels (Cole, 1948) or other large vessels (*B.M.J.*, 1949). A reasonable explanation of the pericarditis in Case 1 seems to be arteritis of the vessels supplying the pericardium—branches of the internal mammary vessels or descending aorta—producing a pericardial infarction. Pericarditis or subepicardial infarction is known to occur in some cases of coronary occlusion, so that vascular lesions can produce such changes. On the other hand, they are not invariable in coronary disease, so that the subepicardial muscle derives part of its blood supply from elsewhere. The vessels providing the supply may be those damaged by the arteritis in Case 1, and possibly in "idiopathic" Case 2 some chance lesion may also have affected them. The rarity of an obvious general cause may be due to the fact that when there is generalized arterial disease the coronary vessels, exposed to constant and severe stresses in unintermittent response to changes in the internal and external environment, will fail earlier than the relatively sheltered vessels of the pericardium. These, on the other hand, may suffer from such diseases of capricious local incidence as temporal arteritis.

Summary

Two cases of acute pericarditis simulating cardiac infarction are reported, one associated with temporal arteritis. Pericardial infarction is suggested as a responsible mechanism.

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ADDENDUM

Since completing the above a further case has been observed and the article by Harrison and Wood (*Brit. Heart J.*, 1949, **11**, 205) has been published. Their Fig. 9 illustrates development of anastomoses via pericardial vessels in coronary artery disease, by which means the blood supply of subepicardial muscle is presumably maintained. Increase of such pericardial anastomoses by talcum insufflation of the pericardium provides a rational therapy in coronary disease and has been performed on three of my cases, without mortality and with some symptomatic relief.

Medical Memorandum

Gangrenous Intussusception

This note records the successful resection of a gangrenous ileo-ileal intussusception in an infant of just under six months, on the third day of his illness.

CASE REPORT

The following pre-operative notes were kindly supplied by Dr. Michael Cutler:

"I first saw the patient at twelve noon on a Saturday, when the mother stated he seemed 'grievy' and not his usual self. He had twice vomited, first at 9 a.m. that morning and again about 11 a.m. After the operation the mother was again questioned and agreed that the child had an attack of screaming, with drawing up of the legs and pallor, at or about the time of the vomiting. It would appear the attack was neither prolonged nor violent, as the mother, an intelligent witness, thought it unworthy of mention when first questioned.

"The first examination was completely negative, except that the child looked rather pale. The bowels had not been open since the previous evening. I attributed the pallor to a severe infection, and fully expected diarrhoea and pyrexia to appear in a few hours. I instructed the mother to give 8 fl. oz. (227 ml.) feeds of half normal strength three-hourly. I saw the child again that evening. By then he had much improved: the pallor had gone and there was no more vomiting. For the second time I sought in vain for an abdominal tumour. The child slept all through Saturday night, and by Sunday morning the mother thought he had recovered. The failure of the bowels to act was attributed to the small feeds and vomiting. I again carefully examined the patient, but could find nothing wrong. I instructed the mother to continue diluted feeds and announced that I thought the trouble was nearly over. I left the child for twenty-four hours, making my next call on Monday morning. One glance at the child as I entered the room was enough—he was sweating, pale, and obviously very ill. The mother told me he had been vomiting severely since Sunday at 9 p.m. and there was a foul odour to the vomitus. I again examined the child and found no abdominal tumour, but the other signs were now conclusive."

This is a case of intussusception unrecognized until the third day. The failure in diagnosis is attributed to absence of the usual physical sign of blood per rectum, and to the striking absence of pain after the first day. There was only one attack of screaming, and that was brief. The vomiting was not profuse until 9 p.m. on the second day. The apparent recovery early on the second day also contributed to the difficulty of diagnosis. The case exemplifies the need for vigilance, as emphasized by Morrison and Court (1948).

On admission, the child's temperature was 100.4° F. (38° C.), pulse 144, respiration 28. He looked pale and ill. The abdomen was resistant to palpation, but when the patient relaxed a firm, sausage-shaped mass could be felt lying across the right lower quadrant, fixed with the axis to the right and upwards. This mass was deep in the abdomen and did not harden with the pains. This failure to harden was explained by the subsequent finding of a gangrenous intussusception.

Operation.—Dr. A. H. Grace administered ethyl chloride and open ether. Pre-operatively a catheter was inserted into the stomach and a quantity of greenish fluid aspirated; the tube was kept in place during the operation. A right paramedian mid-abdominal incision was made, and revealed some clear free fluid. An irreducible, gangrenous intussusception of the small intestine was found. This was resected between clamps, and an end-to-end anastomosis was performed with two rows of interrupted catgut. A small oil-silk drain was inserted into the pelvis and left protruding from the wound, which was closed in layers.

The first day after operation the child was very restless, and vomited a considerable amount of green fluid. A catheter was passed into the stomach for hourly aspiration. He was passing urine normally. Intravenous glucose-saline was administered, and he was given 50,000 units of penicillin four-hourly for nine days. During this time the evening temperature reached 100–101° F. (37.8–38.3° C.). He received hypodermic injections of "nepenthe" 1 minim (0.06 ml.) as required, and 3 ml. of water hourly. On the second day after operation a quantity of stale and bright red blood was passed per rectum, and a little greenish fluid was withdrawn from the stomach. Plasma (200 ml.) was administered intravenously, followed by 200 ml. of Group O blood and normal saline.

On the third day about 200 ml. of gastric contents were withdrawn by hourly aspiration. This was a considerable increase, but the patient appeared to be much better in the afternoon. The intravenous drip was then discontinued and the bowels were opened with a rectal saline.

On the fourth day the patient was much better. Gastric suction was discontinued and he was given glucose by mouth. He was passing urine and yellow, loose motions, and he smiled for the first time since the operation.

On the fifth day he was well, and took small amounts of milk and glucose solution.

On the sixth day the wound discharged during the night. The child vomited one feed, and the bowels were opened. In the afternoon a faecal fistula formed, which closed after five days. Sulphamezathine (sulphadimidine) was given for four days, the dosage totalling 3.25 g. After this the patient became apyrexial, and his progress has since been uneventful.

Acknowledgment is due to Dr. J. McMurray for directing the post-operative treatment with untiring skill, to Dr. M. Graham, and to Sister I. A. Vincent and the nursing staff of the Royal East Sussex Hospital for their loving care, and to Mrs. W. Beaufrere for her help in the arrangement of this account.

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REFERENCE

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Professor Frits W. Went, designer and director of the new Earhart Plant Research Laboratory in California, said that for the first time in the history of experimental biology it was now possible to grow plants under a wide variety of rigidly controllable conditions. All possible climatic factors, such as light, temperature, humidity, and gas content of the air, are simultaneously and independently controllable in the laboratory, which is to be used for experimental work by the California Institute of Technology.

Reviews

COMMON SURGICAL INFECTIONS

Clinical Aspects and Treatment of Surgical Infections. By Frank Lamont Meleney, M.D., F.A.C.S. With foreword by Allen O. Whipple, M.D. (Pp. 840; 287 figures and 241 illustrative cases. £3.) Philadelphia and London: W. B. Saunders Company. 1949.

This book is a companion to the author's treatise on surgical infections, and the two volumes form a comprehensive work. Dr. Meleney considers the commoner infections in each region of the body—the skin, the head and neck, the heart and pericardium, the mediastinum, the lungs and pleura, the peritoneum, and so on—finishing with chapters on surgical septicaemia and war wounds. The scope of the book necessitates a considerable amount of repetition, and it is difficult to read much of it at one time. It is essentially a volume of reference for the practitioner to dip into when he is confronted with a difficult case of infection in any part of the body. There will hardly be any problem on which he will not find some useful word of advice, or some illustrative case which may serve as an example of what to do or what to avoid. Every practitioner would do well to read the account of the case of appendicitis on page 417, which so strongly emphasizes that delays are dangerous.

Every section is complete in itself and provides an account of the relevant pathology and bacteriology, signs, symptoms, and treatment, and a bibliography of the most important books or articles dealing with the subject. The author shows a remarkable knowledge of the literature, particularly the American, English, Canadian, and French journals. The absence of many references to German periodicals is probably due to the dearth of original work on the subject in that country during the last ten years.

Though the book was begun twenty years ago it contains the latest work on penicillin and streptomycin, and gives an account of an antibiotic called bacitracin, on which the author has done considerable research. There is little evidence that this substance is better than or even as good as penicillin, and it does not appear that it is yet available on any scale; that being the case, it is unfortunate that the drug should be given so prominent a place in this record.

There is so much good in this book and in the companion volume that I would suggest the two were made into one small, practical manual. This would be of even greater value to the busy practitioner.

ZACHARY COPE.

PHYSICS IN SURGERY

Physics and the Surgeon. By Sir H. S. Souttar, D.M., M.Ch., F.R.C.S. (Pp. 60. 7s. 6d.) Oxford: Blackwell Scientific Publications.

It is both inherent and axiomatic that surgical, as opposed to medical, methods of treatment should be largely physical in their nature. Records show that from early times surgeons were employing splints, traction, heat, cold, and other measures the use of which demanded some acquaintance with physical principles. This tendency has increased until the present day, when the surgeon is surrounded by complicated machines in which modern physical advances are put to practical use. Furthermore, he is called upon to use radioactive materials which depend upon atomic nuclear disruption for their biological effects. The practical surgeon cannot be expected to have a detailed knowledge of the constructional features of these machines nor of the mathematical profundities of nuclear physics, but at least he should know something of the underlying general principles.

The amount of physics demanded of the medical student is not sufficient to cover this field. To remedy the defect Sir H. S. Souttar has written this small book, which explains in simple language the surgical applications of physics, from elementary levers to radioactive isotopes. The author's interest in this aspect of surgery is well known, and within sixty pages he has managed to include a wide range of authoritative information. The surgical student whose knowledge of physics is deficient or requires revision will find this book admirable for his purpose.

NORMAN C. LAKE.

EARLY DIAGNOSIS

Early Recognition of Disease. Edited by Sir Heneage Ogilvie, K.B.E., D.M., M.Ch., F.R.C.S., and William A. R. Thomson, M.D. (Pp. 134. 10s. 6d.) London: Eyre and Spottiswoode. 1949.

This is one of the handbooks in which are reproduced a series of articles published in the *Practitioner*. Two chapters have been added, one by Professor Moncrieff on diseases of childhood and the other by Professor Sorsby on diseases of the eye. The remaining articles deal with diseases of the heart, lungs, nervous system, digestive system, blood, kidneys, and endocrine glands; and with orthopaedic disabilities, non-specific arthritis in adults, malignant disease, mental disorders, and the complications of pregnancy. A wide selection in a small compass, and all written by recognized authorities.

The preface states that "during the last thirty years a mass of data has accumulated concerning the recognition of disease in its early stages. Much of this, however, has not found its way into the standard textbooks or is not easily available to the practitioner or medical student." For this reason, we are told, the book has been published. This is a reflection upon the standard textbooks and those dealing with the special branches of medicine and surgery. But is it true that these works do not contain all the important information available for the recognition of disease in the early stages? Does this small book give any information of this character which is not discussed more fully in the standard texts? Take any subject—for example, the early recognition of malignant disease of the colon. We are told in this book that it is necessary to make digital, radiographic, and sigmoidoscopic examinations. But did we not all know this before? Are not the standard books readily available to students and practitioners in the medical libraries and bookshops? These and similar questions can easily be answered by the curious reader who is willing to make the necessary comparisons.

Diagnosis is an art which must be learned at the bedside. There is no short cut to the early recognition of disease, and failure to make an early diagnosis often depends more on lack of care than on lack of knowledge, and on the neglect, or apparent inability, of the observer to select and apply special knowledge to the individual case. Professor Moncrieff has hit the nail on the head when he writes in the concluding chapter: "Complete physical examination . . . is the real clue to the early recognition of disease," and, "Skill and experience with children is an essential requisite for the early recognition of disease." And this applies to adults also.

G. E. BEAUMONT.

CLINICAL DIAGNOSIS

Diagnostik durch Sehen und Tasten. By H. Kahler. (Pp. 253; illustrated. 13s. 6d.) Vienna: Springer. 1949.

Central European medical literature has a tendency to the bizarre rather than the basic, and Dr. Kahler's book on bedside methods is therefore welcome. The author was a pupil of Chvostek, and the academic pedigree of "Diagnosis by Sight and Touch" is therefore unexceptionable. The book is arranged by regions, and under each regional heading the features to be sought or examined are enumerated.

The pages devoted to methods of examination are relatively few and are unbalanced. For example, in discussing palpation of the abdomen the author makes no mention of the everyday matter of palpation in children, but finds room for a reference to "the superficial and deep palpation of Hausmann, the diaphragmo-inspiratory palpation of Obrastzow, the double-handed gliding palpation of Martini . . . a similar procedure of Lejars and Laqueur."

There are nevertheless many features of interest among the descriptions of signs—for example, an account of the

mechanism of neck-vein pulsation. But again there are grave deficiencies. The palpation of vocal fremitus and of tracheal displacement are both unmentioned. The almost useless section on the cervical lymph-nodes does not distinguish the various groups. The book is most inadequately illustrated, and the seventeen photographs show the less common of the subjects discussed. The reader who is in a position to be critical may find some interesting gleanings. He may also be pleased to take advantage of the extensive bibliography, which gives references to many classical descriptions.

JEFFREY BOSS.

GERMAN MIDWIFERY

Lehrbuch der Geburtshilfe. By Professor Heinrich Martius. (Pp. 1,196; illustrated. M. 72.) Stuttgart: Georg Thieme. 1948.

Martius's *Textbook of Midwifery* is a typical German work, with excellent paper and print. The illustrations are adequate and good: many of them are familiar and have been copied from those already well known in Germany, and others resemble the illustrations found in De Lee and Greenhill. Professor Martius has a great reputation for ingenuity in illustrations, and the new diagrams are of the same high level as those found in his textbook on gynaecology. There are relatively few references to original papers, a disappointing omission in a volume of this quality, which will surely rival the works of Stoeckel and Guggisberg.

This review is a convenient opportunity to point out the wide divergences between German obstetrics and the practice in the United States and Great Britain. In Martius's book there is no evidence whatsoever of the influence of progress in antenatal care upon German midwifery. It is difficult to understand why German obstetricians have persistently neglected antenatal supervision and have ignored the great contributions made in the subject in this country. As a result this textbook is entirely different in style from modern British publications. Moreover, little attention is paid to the problems of the Rhesus factor, and the description of contracted pelvis is likely to be severely criticized both in the United States and in Great Britain. The book has the usual German emphasis on malformations of the foetus and upon rare deformities of the uterus. The German means of controlling post-partum haemorrhage are well illustrated, and it is interesting that the methods have never found favour here. In Germany and Central Europe Martius's book will have a wide appeal, and the author is to be congratulated on his industry and his great power of expression.

WILFRED SHAW.

IMMUNITY TO SYPHILIS

Racial Variations in Immunity to Syphilis. A Study of the Disease in the Chinese, White, and Negro Races. By Chester North Frazier and Li Hung-Chiung. (Pp. 122. 14s.) Chicago: University of Chicago Press. London: Cambridge University Press.

Both the main title and the subtitle of this little book are misleading, for little is said about true immunity, and, although the study includes Chinese, white, and nego males and females, it only refers to selected groups of the populations of Peking and Baltimore. A comparison of these three groups may, as the authors admit, be prejudiced by the fact that the Peking group were probably undernourished and short of vitamins, whereas these factors were unlikely to apply to the Baltimore groups, either white or negro. Not only are these groups compared, but the two sexes also, a matter of some importance, as it is generally agreed that syphilis is a milder disease in the white woman than in the white man. Possibly the most important point to emerge from this study is that syphilis in the male Chinese assumes very much the same pattern as it does in the white woman; this agrees with the general make-up of the Chinese people, which is more related to that of the female than the male. Of the various manifestations of the disease the Chinese are particularly susceptible to acute meningitis, to skeletal lesions, and to skin lesions in the secondary stage, but are much less prone to late neurosyphilis than the other groups. On the other hand, the negro is more commonly affected by cardiovascular syphilis, especially in the form of aneurysm. These authors consider that all the evidence is against the concept of tropism in so far as dermotropic and neurotropic strains of *Treponema pallidum* are concerned. Within its sphere the book is full of interest, but the student of syphilis would have appreciated information about more races, more areas and climates, and more forms of spirochaetal infection such as yaws, bejel, and pinta. So little is known about syphilis in China that detailed information on congenital syphilis in that country would have added much to the value of the study. There are 27 tables containing a mass of statistical detail, 13 figures, and an ample bibliography.

T. E. OSMOND.

ADVANCES IN PUBLIC HEALTH

Modern Trends in Public Health. Edited by Arthur Massey, C.B.E., M.D., D.P.A., with 23 Contributors. (Pp. 581; illustrated. £2 10s., plus 1s. 6d. postage.) London: Butterworth. 1949.

At a time when the duties of local authorities in relation to public health have been radically altered by the law, Dr. Massey has performed a valuable function in producing this useful volume. The twenty-three papers are by persons well versed in the particular aspects of preventive medicine they discuss. The objection to this form of publication is that a certain lack of balance is inevitable, and the reader must endeavour to assess the relative importance of the numerous subjects that these papers cover.

The manner in which public health must be integrated with other forms of social endeavour is laid down by Professor Crew in the section headed "Future of Social Medicine," which is contained in the chapter with the arid title, "Social Medicine as an Academic Discipline." I was disappointed, however, to find in this section no reference to family life as the basis of personality. Dr. Odlum has contributed an excellent article on the mental health aspects of public health, and W. Edwards has written an equally good discussion on the contribution of preventive medicine to general practice. Individual subjects are discussed authoritatively, as in Fraser Brockington's informative article, "Nutrition and Public Health," and Tattersall's section on tuberculosis. Tattersall rightly gives an early place to the value of B.C.G. vaccine, about which he states that "an officially sponsored supply of the vaccine is expected to be available for selected groups of patients in the near future." Professor Cruickshank's "Recent Laboratory Contributions to Public Health" is a valuable summary. Paul's account of day nurseries will, I fear, leave doubts whether the staffs of these units are always capable of carrying forward Margaret Macmillan's work.

C. O. STALLYBRASS.

SEXUAL INVERSION

The Invert and his Social Adjustment. By "Anomaly." With an introduction by R. H. Thouless, M.A., Ph.D. Second edition. (Pp. 290. 8s. 6d.) London: Baillière, Tindall and Cox. 1948.

The first half of this book is a reprint of a work published in 1927. It was widely appreciated as an authoritative discussion of the personal problems of the male invert and as a portrait of a fine man with exceptional literary gifts. The "sequel" now added records some changes of opinion and discusses broader questions such as homosexuality as an instrument of political blackmail, as a theme in literature, and as a phenomenon in prisons, internment camps, and the Services. The author is an invert (though not a medical man), and his observations now extend over nearly fifty years.

The author accepts the Roman Catholic rule that "the sex impulse can be licitly indulged only in marriage, and then only without interference with the natural physiological consequences." This does not invalidate his discussion, and the existence of other viewpoints is recognized. The author thinks that the wisest course for an invert is complete abstinence from

any form of sexual relation, even platonic. He knows that this is counsel of perfection, and thinks that legal penalties should attach only to actions corresponding to those for which normal men are punished.

The frequency of inversion has probably been exaggerated through failure to distinguish it from bisexuality, and the author estimates that the percentage of inverts in the male population is not more than five. This figure may seem high, but lower estimates may be due to lack of skill on the observer's part. The author found no evidence for the opinion that seduction plays a significant part in causing inversion—an opinion reminiscent of the attribution of tumours to trauma. Of his more recent findings, perhaps the most interesting is that sexual attraction between inverts is extremely rare: a male invert almost invariably desires that his "mate" shall be a completely normal man. The conclusion drawn is that "all psychosexual attraction is essentially heterosexual." The book leaves no doubt that sexual inversion is wholly involuntary or that most inverts—like most normal men—try to live decent and useful lives.

This work will be helpful to specialists, whose knowledge of inversion may be based solely on clinical experience. To general practitioners—and indeed to all who have to deal with young people—it will be invaluable.

RAYMOND WHITEHEAD.

DELINQUENT CHILDREN

Children in Need. By Melitta Schmideberg, M.D.(Berlin). Introduction by Edward Glover, M.D. (Pp. 196. 12s. 6d.) London: George Allen and Unwin. 1949.

Another book on the difficult and delinquent child seems superfluous, but this volume, by an experienced worker at the Institute for the Scientific Treatment of Delinquency, is well worthy of study. It supports the familiar theses that home is best, foster parents are better than institutions, and that institutions (if they must be used) should be small, humanitarian, and staffed by intelligent and sympathetic trained people. The author stresses that reports of committees, laws, and regulations do not necessarily achieve all that is wanted, though they may be steps in the right direction. She points out that even now there is too little recognition of the needs of individual children, and too great a tendency to move children to an institution as the easiest course. The trouble and money might be better employed improving the child's home, to which he will probably have to return eventually. Institutions are in many cases too Victorian in outlook and organization, as they were often founded by charity with the object of uplifting the lower classes and imposing a patronizing and highly religious atmosphere on the inmates.

If a child cannot be kept at home the parents can be helped and taught so that the child can return at the earliest possible moment. Earlier and more effective psychological treatment of the child is urgently necessary, and proper training—not merely laundry work and scrubbing floors—should be given to the adolescent to fit him for a worth-while job when he returns to the world.

The author has her prejudices—for example, against public schools, which she looks at too much from the neurotic child's viewpoint—but she presents her case in an interesting and persuasive way which may convince readers that, in spite of improvements and plans, all is not yet well in the management of delinquent children.

R. G. GORDON.

It is good to see the publication of French clinical lectures again. Dr. H. Grenet is already well known for his contributions in this style, and his new edition of *Conférences Cliniques de Médecine Infantile* (pp. 275; illustrated; no price; Paris: Vigot Frères; 1949) provides a good opportunity for offering a new welcome to an old friend. Fourteen lectures are included, mostly about disorders of the newborn or young infants. The cases chosen as illustrations are graphically described, and the discussions are interesting and practical. Differences from British teaching are not difficult to find—for example, the discovery of a tumour in congenital pyloric stenosis is not regarded as important. But it would be a dull world if all physicians agreed, and it is stimulating to read passages with an approach completely different from the traditional British one.

BOOKS RECEIVED

[*Review is not precluded by notice here of books recently received*]

A Synopsis of Medicine. By Sir Henry Tidy, K.B.E., M.A., M.D., B.Ch., F.R.C.P. 9th ed. (Pp. 1,243. 30s.) Bristol: John Wright. 1949.

The Invisible World. By H. Carrington, Ph.D. (Pp. 123. 9s. 6d.) London: Rider. 1948.

Der Arzt der Persönlichkeit. By E. Speer. (Pp. 285. M. 26.) Stuttgart: Georg Thieme. 1949.

Über Weichteiltuberkulose. By M. Birkenfeld. (Pp. 45. M. 6.) Stuttgart: Georg Thieme. 1949.

Die elektrochirurgische Behandlung der Tuberkulose. By H. Brügger. (Pp. 76. M. 10.80.) Stuttgart: Georg Thieme. 1949.

Neuere Tuberkuloseforschung I. By R. Griesbach. (Pp. 112. M. 6.) Stuttgart: Georg Thieme. 1949.

Die Lungentuberkulose. By H. Gissel and P. G. Schmidt. 2nd ed. (Pp. 264. M. 26.50.) Stuttgart: Georg Thieme. 1949.

Die Erkrankungen des Darmes. By W. Zweig. (Pp. 253. M. 22.) Stuttgart: Georg Thieme. 1949.

Experimentelle Untersuchungen über Rontgeneffekte und chemische Effekte auf die pflanzliche Mitose. By K. Hohl. (Pp. 87. M. 6.) Stuttgart: Georg Thieme. 1949.

Behandlung Innerer Krankheiten. By F. Hoff. (Pp. 471. M. 25.) Stuttgart: Georg Thieme. 1949.

Gemeinsame Erkrankungen aus der Inneren Medizin und Chirurgie. By W. Kanert and K. A. Koelsch. (Pp. 500. M. 35.) Stuttgart: Georg Thieme. 1949.

Lehrbuch der Stimm- und Sprachheilkunde. By R. Luchsinger and G. E. Arnold. (Pp. 431. 72s.) Vienna: Springer. 1949.

Die Insulin-Lipodystrophie. By F. A. Kehrer. (Pp. 43. M. 4.50.) Stuttgart: Georg Thieme. 1949.

Le Syndrome Hépato-Ovarien. By J. A. Huet and others. (Pp. 63. 200 francs.) Paris: L'Expansion Scientifique. 1949.

Algies Vertébrales d'Origine Statique. By S. de Seze and others. (Pp. 55. 200 francs.) Paris: L'Expansion Scientifique. 1949.

L'Humeur Aqueuse. By L. Alaerts. (Pp. 87. No price.) Brussels: Acta Medica Belgica. 1948.

Introduction à l'Étude de l'Endocrino-Psychiatrie. By A. M. P. Abély. (Pp. 184. No price.) Paris: Société d'Édition d'Enseignement Supérieur. 1949.

Vorschlag zu einer Leicht Durchfuhrbaren Krebs-Prophylaxe. By R. Stöger. (Pp. 64. No price.) Vienna: Wilhelm Maudrich. 1949.

Ayurved-Vigyan-Mimansa. By P. Jha. (Pp. 80. No price.) Cawnpore: Brahman Press. 1948.

Überwärmung als Heilmittel. By H. Lampert. (Pp. 180. M. 15.) Stuttgart: Marquardt. 1948.

Dosis und Wirkung. By H. Druckrey and K. Küpfmüller. (Pp. 130. No price.) Berlin: Werner Saenger. 1949.

Tratamiento de las Meningitis Agudas Supuradas en el Niño. By S. Bonaba, A. Carrau, and others. (Pp. 107. No price.) Montevideo, Uruguay: Garcia Morales-Mercaut. 1948.

Lehrbuch der Haut- und Geschlechts-Krankheiten. By W. Schönfeld. 5th ed. (Pp. 458. M. 24.) Stuttgart: Georg Thieme. 1949.

Die Permeabilitäts-Pathologie. By H. Eppinger. (Pp. 755. £7 2s. 6d.) Vienna: Springer. 1949.

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PAVLOV AND CONDITIONED REFLEXES

In the opening pages of this issue Professor E. D. Adrian describes the life and work of Ivan Petrovich Pavlov, who was born on September 14, 1849. It is perhaps not common knowledge that Pavlov was already world famous as a physiologist and the recipient of a Nobel prize for his work on the processes of digestion before he became seriously engaged in his researches on the conditioning of innate reflexes—work which was to extend his fame far beyond the physiological and even the scientific world and to become the subject of often bitter controversy among philosophers, moralists, and educationists. Professor Adrian has sketched from his own memories some of the personal qualities of this great figure. All who had met him speak of his sincerity, energy, and enthusiasm and his strenuous adherence to the truth as he saw it. Under the Tsarist regime his professional career was hampered at times by his uncompromising criticism of policies which he thought wrong. The confirmation of his appointment as professor of physiology in the Military Medical Academy at St. Petersburg in 1895 was held up for two years, largely because he made quite plain his disagreements with the Academy's Rector. After the revolution the Soviet Government, it is said owing to the personal intervention of Lenin, gave every support to Pavlov's work, but this did not deter him from voicing his disapproval of what he thought were its faults. In scientific work he was equally outspoken, but, since he applied the same thorough criticism to his own past work as to the work of others and was generous in his appreciation of sound results wherever obtained, his vehemence made few enemies. It may be that in the future more attention will be paid to some of his earlier researches and that the method of conditioning stimuli and the facts elicited therefrom will be judged more important than the behaviourist "philosophy" others have based on these experiments, but it can hardly be doubted that his work on conditioned reflexes will have a permanent place in the history of human thought.

The basic facts of the conditioned reflex are now a part of elementary biological education. All Pavlov's own work was done on dogs, and much of it with the salivatory response.[1] Food placed in the animal's mouth produced a flow of saliva (unconditioned reflex): if placing food in the mouth was constantly associated with some other stimulus, this stimulus alone would after a time cause salivation (conditioned reflex). The associated or conditioned stimulus could be a constant property of the food (for instance, its smell or appearance at a distance); something less intrinsic, such as the dish on which it was placed or the sound of that dish being filled; or it could be something quite artificial, such as the ringing of a bell or a flash of light. Pavlov's interest was directed to the study of stimuli in this last group, to which the term "conditioned reflex" generally refers. In reporting his earlier results Pavlov wrote, "We see here facts which . . . seem to imply intelligence," and for over 30 years he and his associates investigated and elaborated these facts. They insisted on the study only of observed and verifiable physiological responses to the stimuli they applied, and they denied the need for any speculation on the animal's subjective state. Pavlov himself only applied his findings to man in the most general terms, though he was hopeful that the method might bring forward useful facts for human psychology; he certainly claimed that it was one which made possible a physiological approach to "mental" phenomena.

Such an approach was clearly indicated in the study of animal behaviour and the investigation of "intelligence" in animals which was taking place at the turn of the century, particularly in the United States, where Thorndike's[2] work acted as an incentive. Moreover, it had attractions for the growing school of human psychologists who were in revolt against the arid "introspectionist" attitude and were in search of a psychology based on the study of behaviour "without the terms consciousness, mental states, mind, content, will, imagery, and the like." Both the methods and the implications of Pavlov's work appealed to J. B. Watson,[3] who, trained in the study of animal psychology, now attempted to analyse human conduct in the same way. The principles of the conditioned reflex thus became a mainstay to the behaviourism which Watson elaborated. This extremely limited conception of the springs of human conduct, which formally denies the existence of sensation, feeling, and thought because they give rise to no direct observable behaviour and then has to employ the quibble of a "verbal report" to admit them—speaking being observable behaviour—has only a very tenuous connexion with Pavlov's work. But the latter continues to possess great potentialities for the physiological analysis of adaptive behaviour. Its findings are on a different plane from those of

[1] Pavlov, I. P., *Lectures on Conditioned Reflexes*, 1928, London.
[2] *Animal Intelligence*, 1898, New York.
[3] *Behavior. An Introduction to Comparative Psychology*, 1914, New York.
[4] *A Study of the Knee Jerk*, 1902, Ph.D. thesis, University of Philadelphia.

introspection, and it seems unnecessary to try to oppose the two. It is interesting that one of the earliest observations on conditioning was made by Twitmyer[4] on the human knee-jerk before Pavlov's main work was under way. He reported that this reflex became conditioned to a sound which would then evoke it without any stimulation of the patellar tendon. The subjects actually made "introspective reports" of the experience, and there was apparently no conscious volition or anticipation of the reflex jerk, so that in this case at any rate the conditioning must have occurred in a different part of the nervous system from that in which conscious adaptive behaviour takes place.

So far Pavlov's work seems to have less application to clinical medicine than have the results of other contemporary neurophysiological studies. The researches of Sherrington, of Adrian himself, and of many others now working along lines indicated by these pioneers frequently elucidate the problems encountered in a neurological clinic, but it is quite unusual to formulate a case in terms of conditioned reflexes; even in psychiatric practice such a formulation is rarely made in this country. The idea of conditioning stimuli, especially in the emotional sphere, is inherent in much modern psychiatry, but formal behaviourism seems on the wane. Nevertheless, the harvest of Pavlov's work will not be complete until the facts his method is still accumulating can be satisfactorily related to the physiology and anatomy of the nervous system. When that is achieved neurophysiology and neuropsychiatry will both have gained information of fundamental importance.

FREEDOM FROM WANT

Freedom from want was one of the results which President Roosevelt hoped that peace would bring. Most educated people, however, are now aware that, unless the production of food is increased at a faster rate than that of the world's population, attempts at social improvement are not likely to succeed. The elements of the problem are simple: world population is increasing at the rate of at least 20,000,000 people a year, an average of two every three seconds. The two may well become three or more as science advances, social services improve, and bodies such as the World Health Organization become fully operative. Although some areas are relatively empty, others are already overpopulated, and it is just in these areas, such as the West Indies, that the population increase is of the order of 2% per annum. If world food supplies are not progressively increased, if the growth of population is not slowed down by control of births, or if mass migration does not take place, then one or more of Nature's checks will be automatically applied in the form of famine, war, or epidemic disease. If freedom from want is to be attained, much more than the application of the natural sciences to food production will be required: superstitions, religious scruples, racial customs and prejudices—based often on the unconscious and irrational—are as important as, perhaps more important than, economics and politics.

It is not surprising that some bewilderment exists at the present time. On the one hand the Royal Commission on Population[1] has no hesitation in recommending that a replacement size of family is desirable in Great Britain, though it finds it by no means easy to weigh the factors entering into its conclusions; "imponderable" elements in the situation are at least partly responsible for this. On the other hand the example of an island such as Malta may be cited, where unless food or money is poured in from abroad or large-scale emigration is encouraged the present population cannot be supported. Many, too, will have read with some alarm such works as *Our Plundered Planet*[2] or *The Road to Survival*.[3]

In these circumstances Sir John Russell's authoritative review of the problem in his presidential address to the British Association on August 31 at Newcastle-upon-Tyne is of particular interest. Expansion of the world's food supplies depends, he believes, on extension of the food-producing areas, more intensive cultivation of the areas already used, and reduction of the present heavy wastes and losses. The food-producing areas represent at present an average per person of about one acre and a half, whereas if all the "climatically suited" areas were under cultivation there would be about five acres for every person. Agricultural science is now in a position to convert much marginal land into good farm land, and with control of pests and disease among plants and animals, destruction of weeds, and increased use of fertilizers there is every possibility of producing far more food than at present. Then, too, recent investigations have shown that only the best stock need be used for breeding. Artificial insemination from sires of good stock is now regularly practised, but there is evidence to show that fertilized ova from a particular mother can be artificially implanted into the uteri of other cows. One cow could thus become the mother of 75,000 calves. Unfortunately Sir John Russell scarcely touches on the human side of the problem, beyond the reminder that food will not be produced by the more advanced nations merely from a sense of duty. If Western standards of food are required by less advanced peoples they must also use Western standards of restraint.

[1] Report of Royal Commission on Population. (Cmd. 7695.) London: H.M.S.O. See leading article in *British Medical Journal*, 1949, 1, 1127.
[2] Osborn, F., *Our Plundered Planet*, 1948. London: Faber and Faber.
[3] Voigt, W., *The Road to Survival*, 1949. London: Victor Gollancz.
[4] *Freedom from Want*, a symposium edited for the American Association for the Advancement of Science, by E. E. DeTurk, 1948. Waltham, Mass.: Chronica Botanica Co.
[5] *Émile, ou de l'Éducation*, 1762, Paris.

Another useful contribution on this subject is a symposium of the American Association for the Advancement of Science.[4] Agricultural experts and economists have shown that by using our present cultivated lands more efficiently and by bringing certain new lands into use it would be possible to double the world's food production by 1960. This would mean that more of the red and lateritic soils of the Tropics and sub-Tropics, which together constitute 19% of the earth's surface, would have to be used. That this task is none too easy has been shown by the difficulties of growing even groundnuts and sunflowers in Tanganyika. Nevertheless in the U.S.A. the increase in rice per acre has been almost unbelievable, and an increase of only 10% in yields in China and Burma would supply food for some additional 58,000,000 people. The professor of economics at Harvard, Dr. J. D. Black, emphasizes the fact that as undeveloped communities modernize their economics their populations, while initially rising, soon begin to fall. Japan is now rapidly passing through such a cycle. However, even the rate of decrease in the birth rate of Japan is not rapid enough by itself, and the real demographic need of Asia and also of many areas in Africa and the West Indies is to devise ways by which the diffusion of the small family pattern may be quickened among peasant populations. H. R. Tolley, the Director of Economics and Statistics of FAO, puts his finger on one of the crucial difficulties: "If a particular nation needs food imports exporting countries must expand their output to meet this demand. Simultaneously the importing nation must boost its production of other goods to trade for the food it imports." Unfortunately he does not explain what other goods the African peasant, armed with a hoe, can possibly supply to exporting countries such as the U.S.A., where good imitations of everything down to a Camembert cheese are already available.

Although so far no practicable crop or cropping system has been found for restoring to the soil either the depleted nitrogen or the organic materials which are slowly but surely lost as a result of constant cultivation, nevertheless the Director-General of FAO believes that civilization can reach safety: it need not succumb in the desperate struggle of too many people trying to live on too limited resources. Prophecy is of course dangerous. Writing in 1762, at the very dawn of the industrial revolution, Jean Jacques Rousseau,[5] no foolish observer of the contemporary scene, could solemnly declare that in a few years' time Europe would be depopulated, a desert inhabited by wild beasts. In 1898 Sir William Crookes, at a meeting of the British Association in Bristol, asserted that by 1930 the world would be starving. Both these prophecies failed to come true for reasons quite unforeseen by their authors. One reason for controlled optimism is that the growth of scientific knowledge will not cease with this current fiscal or calendar year. Fungi and bacteria, for instance, synthesize not only antibiotics but vitamins and amino-acids. It may be that in the course of time the discovery will be made that if given the right encouragement they could produce something much more substantial.

PENICILLIN-RESISTANT STAPHYLOCOCCI

Although it has been known for eight years that staphylococci can be made *in vitro* to acquire a high degree of resistance to penicillin, strains possessing such resistance were very rarely encountered in patients during the earlier part of this period. They then began to be found, chiefly in patients who had undergone treatment with penicillin, and it was at first supposed that the strains concerned had acquired resistance by the same mechanism as that which had already been shown to operate *in vitro*. It was chiefly owing to the work of Spink and Ferris[1 2] that the existence of two kinds of resistant staphylococcus came to be recognized. The artificially resistant, which can be produced in the laboratory, has apparently little or no counterpart in the clinical field, and is in any case of little practical importance owing to its diminished virulence. The naturally resistant type, on the other hand, is fully virulent and owes its resistance to its property of forming penicillinase, an enzyme which destroys penicillin. It is this type which is found in patients whose treatment has failed, and is now also being encountered with increasing frequency in infections of many kinds, often before any treatment has been given.

The most definite and perturbing information about the recent behaviour of these staphylococci is that obtained by Dr. Mary Barber as the result of observations made at the Hammersmith Hospital; she found that the frequency of occurrence of such resistant strains was in three successive years 14, 38, and 59%. It seemed probable that cross-infection within the hospital accounted at least in part for this increase, and subsequent studies on out-patients have shown that among them the frequency of resistant strains is much lower. The importance of this distinction is confirmed elsewhere in this issue by Dr. G. B. Forbes, who studied strains from both in-patients and out-patients at the same hospital and showed that resistant strains were over five times as common among the former. He also found that 23 out of 50 ward nurses were nasal carriers of resistant pathogenic strains, a fact which must have an important bearing on the occurrence of infections due to such organisms. One comment which must be made on such observations is that the wearing of masks,

[1] *Science*, 1945, **102**, 221.
[2] *J. clin. Invest.*, 1947, **26**, 379.
[3] Bellamy, W. D., and Klimek, J. W., *J. Bact.*, 1948, **55**, 153.

and various other precautions, some of which have been introduced or at least modified with a view to greater efficiency within the past ten years, seem not to be having all the effect they should.

A further contribution to the study of this subject by Drs. Mary Barber and J. E. M. Whitehead also appears in this issue. It is concerned with staphylococci from 100 patients, in 24 of whom resistant strains only were found and in a further 11 a mixture of resistant and sensitive strains. Again, in-patients yielded resistant organisms more often than out-patients, though the difference is much less. The findings of chief interest are those resulting from phage typing. This method of identification was applied to the pairs of cultures isolated from the 11 patients having both resistant and sensitive organisms. Though the results are incomplete owing to the fact that some cultures could not be typed, it appears that in only one patient was the phage type of both organisms the same. Still more significant are the findings when phage typing was employed not only for all the resistant strains isolated in this study but for further strains obtained in five other hospitals, 140 in all. Of these as many as 85 belonged to a single phage type and 21 to another, about five typable strains remaining which were assigned to other types. This evidence points to selection as the major factor in causing the increasing prevalence of resistant organisms; most of these, in the London area at least—so far as the hospitals where this investigation took place may be regarded as representative—belong to a single type which must originally have been rare and has flourished in a penicillin-saturated hospital environment which has tended to eliminate other and sensitive types. The possibility that resistant variants may arise by mutation cannot be excluded, and is indeed suggested by the observation that organisms of the same phage type may belong to either category, but the fact remains that such a change cannot be induced *in vitro* except at an extreme stage of habituation, when the organism has become almost unrecognizable owing to the profound changes in its morphology and metabolic behaviour.[3]

Drs. Barber and Whitehead also discuss the quantitative assessment of resistance, pointing out that the heaviness of the infection has also to be taken into account in deciding whether a given concentration of penicillin will arrest the growth of an enzyme-forming staphylococcus. Since this cannot well be determined (except perhaps by quantitative blood culture in a case of septicaemia) the practical advantage of detailed information about the organism in any given case is doubtful. The most useful conclusion to be drawn from these studies is that only a much more vigorous campaign against cross-infection can prevent the frequent occurrence of infections which may be very difficult to treat effectively.

MYXOEDEMATOUS MADNESS

Every physician of experience must be able to recall at least one instance in which he failed to recognize that a patient was suffering from myxoedema. He will be able to remember his dismay when his error was pointed out and his astonishment that such an obvious diagnosis should have eluded him. In the out-patient department it is a commonplace to see patients whose appearance clearly proclaims this malady but in whom it has been unrecognized for years. It is curious that a disease which leaves its stamp so clearly on the patient's face should pass undetected, but the truth of these assertions is once more borne out by Dr. R. Asher's paper on myxoedematous madness in this number of the *Journal*. Of his 14 patients, seen within four years, at least 9 were admitted to hospital without the diagnosis of myxoedema having been suspected.

Dr. Asher's report is naturally concerned with patients in whom mental symptoms were dominant, but his illustrations show that the characteristic myxoedematous facies was not lacking, and he has performed a useful service in drawing attention to a feature of this disease which is obviously common but not widely appreciated. The type of psychotic reaction varied: apathy, confusion, and mental retardation were the rule, but hallucinations were common, and eight patients had delusions of persecution. This inconstant pattern gives some support to the suggestion that myxoedema reveals latent psychotic potentialities and does not induce a "specific" psychosis. The paranoid characteristics have frequently been remarked in the past, and, indeed, the mental symptoms are of the same nature as those of senile deterioration. The effects of cretinism on mental development are well known, and it is the more remarkable that these aspects of myxoedema should suffer such neglect in the textbooks, even in those devoted to psychiatry. That one of Asher's patients had received the label of "paranoid psychosis" from an experienced psychiatrist may explain, but cannot excuse, the general ignorance of myxoedematous madness. The author rightly says that the fault lies in failure to recognize myxoedema rather than the psychosis which accompanies it. To remedy this defect he gives simple directions, ending with the statement, to which all will subscribe, that the only way to make the diagnosis is to know what a myxoedematous patient looks like, and the only way to learn this is to see one. He has found a raised blood cholesterol a useful guide, and the value of his "photographic test" is well illustrated in his article. All physicians will not have shared his experience of having seen cases of myxoedema with a raised basal metabolic rate.

OPHTHALMIA NEONATORUM

In papers[1,2] published in this *Journal* in 1942 and 1944 Professor Arnold Sorsby and his associates drew attention to the value of the sulphonamides in the treatment of ophthalmia neonatorum. In a series of 258 cases treated at White Oak Hospital they reported that with an initial dose of 0.25 g. over 85% were cured within eight days. With penicillin a further advance was made. In an early study in 1945 Sorsby and Hoffa[3] reported only indifferent results with penicillin eye drops in concentrations of 500,

1,000, and 1,500 units per ml., but distinctly better results —21 recoveries in a total of 22 cases—when the concentration was increased to 2,500 units per ml. The drops were instilled at half-hourly intervals for the first three hours and then at hourly intervals for 24 hours. The results as a whole were similar to those obtained with the sulphonamides. Subsequently Sorsby[4] recorded a series of 38 cases with only two failures; the treatment in this series was more intensive, the drops being instilled at intervals of 5 minutes. Clinical cure could be obtained in this way in a matter of hours, this being as great an improvement over the sulphonamides as these in turn were over the older methods. When the concentration of the penicillin was increased to 10,000 units per ml. and the frequency of instillations to one every minute for the first half-hour, the appearance of pus ceased in most cases within half an hour and clinical cure was achieved within 24 hours.[5] Massive intramuscular injections of penicillin also gave good results.

These studies established the systemic administration of sulphonamides and the local application of penicillin as alternative methods of treatment of ophthalmia neonatorum. Sulphonamide therapy has the advantage of being simpler in use, but treatment with penicillin brings about the more rapid cure. Both methods are effective not only against gonococci but against staphylococci, diphtheroids, and all the other common organisms found in ophthalmia neonatorum, and an unexpected finding was that both cured the type of ophthalmia neonatorum caused by a virus. This is important, since the gonococcus, far from being the exclusive cause of ophthalmia neonatorum, is now not even the most frequently found causal organism. Both staphylococcal and virus infections are considerably more common; Sorsby and his associates have found the gonococcus responsible for the infection in less than 20% of the cases in their recent studies. Clinically there is little to distinguish between the different varieties of ophthalmia neonatorum: all may be mild, moderate, or severe infections, and the one substantial difference is the incubation period. When caused by bacteria, the symptoms come on within the first five days of life, but with a virus infection they do not usually appear until the sixth to tenth day. In each group there may, however, be cases that do not conform to these incubation periods.[6] While the sulphonamides appear to act equally effectively on all the causative organisms, penicillin is least active in virus infections, especially if adequate concentrations are not used.

In this issue of the *Journal* Sorsby and Kane report a further study of 151 cases, the object of which was to eliminate relapses. They point out that an unsatisfactory response is not the same as a bad result: in not a single case in their experience has the response to sulphonamide and to penicillin been so poor that anxiety has arisen about the state of the eye, and some of the cases classified as relapses might well have been cases of reinfection. Their bacteriological findings confirm that ophthalmia neonatorum is caused by a number of organisms. When the initial dose of sulphonamide was increased to 0.5 g. the proportion of cases in which a clinical cure was achieved within 1–3 days rose to 68.4%; this compared with 39.3% after an initial dose of only 0.25 g. The authors were not able, however, to reduce the frequency of the relative failures, but there was some indication that with sulphamerazine, used in 24 cases, the frequency of poor responses declined. Penicillin given by mouth alone or combined with intramuscular injections proved disappointing—the results were distinctly inferior to those following intramuscular injections of large doses alone. Likewise no advantage was gained by the combined use of penicillin and sulphonamides. Further investigation is required to determine the best type of sulphonamide to use in the higher dosage now advocated, and to find a less tedious method of penicillin treatment than instillation of drops at intervals of one minute—a procedure trying both to the infant and the nurse.

There are still about 4,000 cases of ophthalmia neonatorum notified each year, and in many of them the danger of blindness is still real. That there has been a great reduction in the incidence of ophthalmia neonatorum can hardly be doubted, but the fact that of late years there has been no definite decline is a sign that existing methods of prophylaxis are unsatisfactory. The system of prophylaxis associated with the name of Credé has two components, aseptic and antiseptic.[7] Prophylaxis by antisepsis—namely, disinfection of the conjunctiva by a drop of silver nitrate—is probably of little value. On the other hand prophylaxis by asepsis—antenatal treatment of the mother by the Credé toilet to prevent infection from entering the eye of the newborn baby—is valid by present-day bacteriological concepts. The persistence of ophthalmia neonatorum therefore raises the question whether obstetricians are as alive to the possible danger of the many varieties of antenatal infection in the mother as they are to the considerably less common danger of maternal gonorrhoea. Prevailing views on the aetiology of ophthalmia neonatorum must be revised if the condition is to be eliminated.

1 *British Medical Journal*, 1942, 1, 323.
2 Ibid., 1944, 1, 353.
3 Ibid., 1945, 1, 114.
4 Ibid., 1945, 1, 903.
5 Sorsby, A., ibid., 1947, 2, 322.
6 —— *J. Obstet. Gynaec. Brit. Emp.*, 1947, 54, 841.
7 —— *Ophthalmia Neonatorum*, 1945. London: Hamish Hamilton.

WHOOPING-COUGH AND BRONCHIECTASIS

Bronchiectasis commonly arises during the first few years of life, the symptoms dating from an acute respiratory infection in early childhood. In the majority of such cases pulmonary collapse has occurred. It is known that when a segment of lung collapses the bronchi in that segment dilate; unless early re-expansion takes place both the collapse and the bronchiectasis become irreversible. Because of the narrow lumen of their bronchi children are more susceptible to lobar or segmental collapse than adults, and collapse occurs in such conditions as simple catarrhal bronchitis,[1] primary tuberculosis,[2] and whooping-cough. As many of these episodes of collapse are unrecognized or pass under the clinical sobriquet of "pneumonia," it is difficult to determine which diseases of childhood are the most frequent precursors of bronchiectasis, but it is widely believed that whooping-cough is the commonest cause. A history of whooping-cough is found in approximately 10% of cases of bronchiectasis in children,[3] and a slightly higher proportion is found in children with collapsed lower lobes.[4]

Although pulmonary atelectasis in whooping-cough was described in the middle of the last century,[5 6] the frequent occurrence of this complication has only recently been recognized. The main reason for this is that segmental pulmonary collapse can be diagnosed with certainty only from clear radiographs taken in both antero-posterior and lateral planes; these may be difficult to obtain in sick children, since reliance must often be placed on portable *x*-ray apparatus. In 1944 Kohn and his colleagues[7] investigated 222 children with whooping-cough by taking radiographs at weekly intervals throughout their illness. It was found that the incidence of pulmonary complications varied directly with the severity of the illness, and in 86.6% of the children considered to be seriously ill the radiographic appearances were abnormal at some stage of the disease. Most of the shadows seen on the *x*-ray films were due to collapse, the right middle lobe being most often affected, and they were usually transient. In no case was there radiological evidence of collapse caused by lymph-node enlargement—a finding which supports the current hypothesis that collapse is due to retention of viscid sputum.

More recently Nicholson[8] has reported on a series of 44 children with whooping-cough who were examined radiologically at intervals. The cases were unselected, the only criterion being that they were ill enough to be admitted to hospital. Four patients died, in three of whom collapse of the lung was demonstrated at necropsy. Nicholson found radiological evidence of segmental or lobar collapse in no less than 39 of his cases. The predisposing factor appeared to be not so much the severity of the illness as delay in admission to hospital after the onset of symptoms. Complete re-expansion of the collapsed lung took place in rather more than half the cases during the first three months of observation and in a further eight during the following six months. No re-expansion was observed after collapse had persisted for nine months. Seven children (21%) out of 33 who were followed up for more than a year had persistent collapse and probably, therefore, bronchiectasis.

This high proportion should dispel any complacency about the treatment of whooping-cough. The recognition of collapse in its early stages is of the greatest importance, for only prompt treatment is likely to be effective. Swift[9] has shown that "aerosporin" (an antibiotic produced by strains of *Bacillus aerosporus*) is of some use in pertussis provided it is given early enough in the disease, and Kinney[10] has reported that inhalations of carbon dioxide (5%) assist patients to expectorate the viscid sputum. A combination of these measures might reduce the incidence of the more serious respiratory complications of whooping-cough. Better still would be prevention of the disease altogether. The preliminary statement on whooping-cough prophylaxis issued by the Whooping-cough Immunization Committee of the Medical Research Council (appearing at page 590 in this issue) is much more encouraging than the report[11] of a trial of whooping-cough vaccine which was published in this *Journal* four years ago.

[1] Ramsay, H., and Scadding, J. G., *Quart. J. Med.*, 1939, n.s. **8**, 79.
[2] Hutchison, J. H., ibid., 1949, n.s. **18**, 21.
[3] Franklin, A. W., *Proc. R. Soc. Med.*, 1944, **37**, 576.
[4] Oswald, N. C., ibid., 1947, **40**, 736.
[5] Gairdner, W. T., *Mon. J. med. Sci.*, 1850, **11**, 122.
[6] West, C., *Lectures on Diseases of Childhood*, 1852, London.
[7] *Amer. J. Dis. Child.*, 1944, **67**, 463.
[8] *Arch. Dis. Childh.*, 1949, **24**, 29.
[9] *Lancet*, 1948, **1**, 133.
[10] *Dis. Chest*, 1947, **13**, 33.
[11] *British Medical Journal*, 1945, **2**, 205.

RESULTS OF COLLAPSE THERAPY

With the present shortage of nursing and domestic staff it is important that valuable sanatorium beds should be used to the best advantage. Simmonds and Martin[1] have recently attempted a statistical evaluation of the results of sanatorium treatment and collapse therapy. Their investigation is based on the study of nearly 4,000 patients discharged from Clare Hall Sanatorium in the years 1937–45. During this period the use of collapse therapy has steadily increased, and for this reason the duration of institutional treatment also increased. The figures show a steady improvement in the 3- and 5-year survival rates throughout the period. The rate for patients who had collapse therapy was surprisingly high, 70% surviving five years. On average about 7% of the patients were lost from observation.

The authors point out that, whatever the treatment, most patients with tuberculosis improve at first, and therefore studies of survival rates must cover at least five years, preferably longer, if they are to be of any value. The worker who undertakes such a long-term investigation has many difficulties. Some, like the movement and dispersal of patients, are inevitable, but others are not; among these may be mentioned the practice at many hospitals of destroying *x*-ray films. Much valuable and unique material is lost in this way, because accurate estimates of the extent of disease can be based only on radiographic evidence. It should not be difficult to arrange that the radiographs of tuberculous patients are preserved.

Simmonds and Martin are well aware of the difficulty of applying statistical methods to tuberculosis problems, but they urge that the attempt should be made so that the clinical observations of different workers may be compared. Unfortunately the Ministry of Health's classification, which they use in their investigation, lacks the precision which is needed to obtain a true comparison. For instance, the authors show that the survival rate of patients in the "T.B.+, Group 2" (B.2) category who had collapse therapy was double that of patients in the same group who had no active treatment. But the limits of this group are so wide that it can include both unilateral and bilateral cases and disease varying in extent from two zones to the whole of both lungs. Hartley, Wingfield, and Burrows[2] showed the close relationship between extent of disease and prognosis, and a classification which gives a more precise indication of the amount of lung tissue affected is badly needed. The revision of the Ministry of Health's classification[3] has left this feature unchanged. Nevertheless the Clare Hall figures show that in a selected group of tuberculous patients collapse therapy undoubtedly improves the prognosis—thus confirming Bentley's[4] observations on patients treated by artificial pneumothorax. Simmonds and Martin are fully justified in concluding that the limited resources at present available should be used for the benefit of those who can be treated with real prospect of improvement; the patients with the best claims for early admission are those with open cavitary disease in whom collapse therapy appears to be practicable.

[1] *Amer. Rev. Tuberc.*, 1948, **58**, 537.
[2] *Brompton Hosp. Reports*, 1935, **4**, 1.
[3] Revision of Section I of the Appendix to Memorandum 37/T (Revised). See *British Medical Journal Supplement*, 1941, **1**, 111.
[4] *Spec. Rep. Ser. med. Res. Coun., Lond.*, 1936, No. 215.

FIRST INTERNATIONAL CONGRESS OF BIOCHEMISTRY

MEETING AT CAMBRIDGE

The first International Congress of Biochemistry, initiated by the Biochemical Society, was held in Cambridge from August 19 to 25. This Congress marks a notable stage in the development of biochemistry as a branch of science covering the ill-defined territory between chemistry and the many branches of biology. The need for an international congress on this subject has been evident for some time, and eight congresses for French-speaking biochemists have already been held since 1927.

The distinguished foreign chemists and biochemists who consented to be honorary vice-presidents, and the names of the lecturers, illustrate the international character of the Congress. Among the vice-presidents were Professor J. B. Collip, of Canada; Professor N. E. Cruz-Coke, of Chile; Academician J. O. Parnas, of the U.S.S.R.; Professor J. Roche, of France; and Dr. D. D. van Slyke, of the U.S.A. Professor M. Florkin, of Belgium, and Sir Robert Robinson, of Great Britain, were among the lecturers. The Congress was opened by the President, Professor A. C. Chibnall, F.R.S. Viscount Addison presided at a reception given to the delegates by the Government during the evening.

The discussions were held in 12 separate groups, as follows: (1) Animal Nutrition and General Metabolism; (2) Microbiological Chemistry; (3) Enzymes and Tissue Metabolism; (4) Proteins; (5) Clinical Biochemistry; (6) Structure and Synthesis of Biologically Important Substances; (7) Cytochemistry; (8) Biological Pigments, Oxygen Carriers, and Oxidizing Catalysts; (9) Hormones and Steroids; (10) Chemotherapy and Immunochemistry; (11) Plant Biochemistry; and (12) Industrial Fermentation.

Vitamin B_{12}

In a discussion on dietary factors in relation to anaemias in the Section on Animal Nutrition and General Metabolism, Dr. K. Folders (New Jersey) said that chemical research carried out with collaborative clinical tests by Dr. Randolph West, of New Jersey, discovered the properties of vitamin B_{12}. The crystals do not melt below 300° C. Emission spectrographic analysis showed the presence of cobalt; thus the molecule was a cobalt co-ordination complex. The red colour and melting point were at least in part associated with the cobalt-complex character. The significance of cobalt as an essential trace element in nutrition could be re-evaluated as the biological functions of vitamin B_{12} became known. Sources other than liver for vitamin B_{12} were being sought, since the natural vitamins were known to occur in numerous animal, plant, and microbiological materials. A red crystalline compound had been isolated from a grisein-producing strain of *Streptomyces griseus*, and this was compared with vitamin B_{12}. Comparative chemical and biological data provided evidence that the crystals from the microbiological source and vitamin B_{12} were identical.

Professor G. R. Cameron, of London, spoke on the pathological types of liver injury. He wished to reduce the complicated patterns of liver necrosis to a few simple components with a geometry of their own. Liver necrosis began with impairment in the functioning of liver cells, such cells being distributed from the trabeculae within the lobules, either singly, or in linear groups, or in clumps. At first there might be no fixed rule in grouping, but sooner or later, usually within a few hours of the onset of the phenomena, a trend of redistribution made its appearance and the necrotic area emerged as focal, zonal, diffuse lobular, or massive lesions. There was reason to believe that this grouping also represented the time sequence of necrosis. All known cases of liver necrosis produced changes which fitted into these groupings. Complications arose with variation in intensity of the causative agent, its power of self-propagation (as in infection with bacteria and viruses), and possible host variations. Analysis had to take into account the disturbances of the vascular relationships within the lobules, the action of the causative agent on the liver cells, the preservation of the biliary mechanism, and possibly the lymphatic integrity of the organ as a whole.

Adrenal Cortex

In the Section on Hormones and Steroids, Dr. G. Pincus (Massachusetts) spoke on studies of adrenal cortex function. He stated that indices of human adrenal cortex function could be obtained by measuring the urinary 17-ketosteroids and neutral reducing lipids, which appeared to vary with the secretion of adrenocortical steroid precursors. Secretory activity of the adrenal cortex was reflected in the changes in the urinary sodium, potassium, and uric acid, and in the blood lymphocytes and eosinophils. Measurements of the diurnal variations of urinary steroid excretion had been made in men and women of various ages, and it was found that the basal output of 17-ketosteroid decreased markedly in older persons, whereas the output of urinary reducing lipids did not. The diurnal variation of each changed with age. Stress procedures or the administration of adrenocorticotropin, which stimulated adrenocortical secretion, were reflected by significant changes in the various blood and urinary indices of healthy men of various ages. Response in terms of these indices to stress or to adrenocorticotropin administration occurred in psychoneurotic patients, but was absent or diminished in most schizophrenic patients. The latter were fairly responsive to adrenal cortex extract, indicating that adrenal cortex response was largely defective in the schizophrenics. This did not appear to be a function of the nutritive state of the schizophrenic patient. The significance of derangements of pituitary-adrenal function in schizophrenia was discussed and the effects of some therapeutic procedures were presented.

It is impossible to report more than a fraction of the large number of discussions held by the Congress. The range of subjects is indicated by the 12 sections already mentioned, and the individual topics varied from a study of acetylcholine metabolism to brewing and yeast production.

During the Congress the University of Cambridge conferred honorary doctorates of science on Viscount Addison, Professor Cori (U.S.A.), Sir Charles Harington, Professor Linderström-Lang (Denmark), Professor Tiselius (Sweden), and Professor Tréfouël (France).

WHOOPING-COUGH PROPHYLAXIS

PRELIMINARY REPORT

The following preliminary statement has been issued by the Whooping-cough Immunization Committee of the Medical Research Council.

In view of the conflicting reports on the efficacy of pertussis vaccine in whooping-cough prophylaxis the Medical Research Council was asked by the Ministry of Health to investigate the problem and report on the value of prophylactic immunization against whooping-cough of children in England and Wales. As part of the investigation the Whooping-cough Immunization Committee organized a series of controlled field trials in which the experience of children inoculated with pertussis vaccine could be compared with that of control children. The results of some of the early trials have already been published (McFarlan, Topley, and Fisher, *British Medical Journal*, 1945, **2**, 205). The evidence obtained suggested that the pertussis vaccine used in these trials was of no value in whooping-cough prophylaxis.

Further large-scale trials have now been carried out in collaboration with the medical officers of health of Oxford, Manchester, Tottenham, Wembley, Edmonton, Leeds, and West Ham, using a number of different vaccines of both British and American origin. Each trial was planned in a similar manner. Children, mostly between the ages of 6 and 18 months, whose parents agreed that they should take part were divided by the method of random sampling into two groups. The children in one group—the test group—were inoculated with the pertussis vaccine under trial, while those in the other group—the control group—were inoculated with an "anticatarrhal" vaccine containing no *H. pertussis*. After inoculation the

children in both groups were kept under close observation for a period of at least two years by monthly home visits made by specially appointed nurse-visitors. Those children who came into known contact with whooping-cough or who developed symptoms which might be those of early whooping-cough received special visits in order that a bacteriological diagnosis might be made. As it was essential that observers should not be influenced in their clinical assessment of the disease, efforts were made to ensure that neither the doctor, nor the nurse-visitor, nor the parents should know whether the child under observation was in the test or the control group.

Seven of the early trials, comprising a total of 4,691 test and control children, have now been in progress for over two years, and from a preliminary analysis of the results the following general conclusions may be drawn:

(*a*) In each trial the random allocation to test and control produced two equivalent groups of children, comparable in age, sex, duration of breast-feeding, size of family, and incidence of infections other than whooping-cough.

(*b*) In six of the trials the incidence and severity of whooping-cough in the test groups were appreciably less than in the control groups. In the seventh trial the results were only slightly more favourable in the test group.

(*c*) There was considerable variation in the prophylactic potency of vaccines from different sources, and there was probably also some variation in the potency of different batches of vaccine from the same source.

(*d*) One particular type of vaccine, not at present readily available, was found to give decidedly better protection against the disease than any of the others tested.

The reason for variations in the prophylactic potency of these vaccines is not clear, nor is there yet available a conclusive laboratory method of assay by which this property of a vaccine can be accurately assessed, but an investigation is in progress in which the prophylactic value in children of a number of different vaccines is being compared with their immunizing properties as shown by laboratory tests. With this aim in view trials have already been begun in Manchester, Oxford, Cardiff, Poole, Walthamstow, and Leyton.

No investigation has so far been made of the value of combined pertussis-diphtheria prophylactic, as it was considered desirable to avoid the inclusion of any factor that might complicate the issue and do nothing that might possibly harm the diphtheria immunization campaign at a stage when the true value of whooping-cough immunization was unknown. This preliminary statement has been prepared on account of the interest shown by health authorities in the outcome of these investigations. A detailed analysis is now being made and should be ready for publication early in 1950.

Members of the Committee and the medical officers of health concerned wish to record their gratitude to the many thousands of parents who have collaborated and are still collaborating in the investigation and who, when control groups have been essential, have volunteered to take part in the full knowledge that their children would not necessarily receive pertussis vaccine.

ROYAL MEDICAL BENEVOLENT FUND

In his annual report on the Royal Medical Benevolent Fund the chairman of the committee of management, Mr. R. M. Handfield-Jones, points out that the inauguration of the National Health and National Insurance schemes does not mean that the need for benevolence has ceased to exist either within the ranks of the medical profession or outside them. He gives several poignant examples of distress amongst elderly doctors and their families. During the year the income of the Fund from invested capital was £13,068, and from subscriptions and donations £23,900. A sum of £32,000 was voted in relief of poverty and distress, some of it in the form of regular annual grants to beneficiaries of many years' standing, some in the form of single grants to meet a case of illness or misfortune, and some again in the form of educational grants for doctors' children. The Fund has now a house near Wimbledon Common where 12 elderly ladies, beneficiaries of the Fund, who were previously living in loneliness are lodged in comfort. Mr. Handfield-Jones reminds the profession that the Fund has never made a public appeal; it has resisted the temptation to be "This Week's Good Cause," believing that an honourable and learned profession ought to be able to deal with its own casualties and help its lame dogs over stiles. He makes a warm acknowledgment of the continuing help of the British Medical Association through its Charities Committee and through the work of its Divisions and Branches, and also that of the Medical Insurance Agency, which "continues, as if with a touch from a magician's wand, to present the Fund with seven-year covenants which magnify the gifts twofold." The treasurer of the Fund, Dr. C. L. Batteson, points out the need for larger grants in individual cases. The former grants of £26 or £40 a year are obviously inadequate in present circumstances, and the committee is in a position to vote grants of £2, £3, or £4 a week in exceptional cases of distress. Legacies during the year totalled £21,670.

At the 113th annual meeting of the Fund Lord Webb-Johnson was elected president, and Mr. Victor Riddell honorary secretary. The address of the Fund is 1, Balliol House, Manor Fields, Putney, S.W.15.

MEDICAL DEFENCE UNION

The annual report of the council of the Medical Defence Union to its members has been distributed recently and will be considered at the annual meeting which is to be held at 49, Bedford Square, London, W.C., on Tuesday, September 20, at 3.15 p.m. The report puts forward proposals about increasing the rates of subscriptions. These increases are necessary, in the council's view, because of the considerable deficits in the Union's income and expenditure for three consecutive years, and because of the probability that these deficits are due to continuing factors and not to exceptional misfortunes unlikely to recur.

If the contention that the causes of the Medical Defence Union's unfavourable experience are likely to be permanent is a well-founded one, it may be surmised that no long period is likely to elapse before the two sister societies follow the lead of the Medical Defence Union. Meanwhile it may be noted that the increased rates are not to apply, on the council's suggestion, to new members during their first three years of membership. This is a helpful concession to junior members of the profession.

The Minister of Food has approved for publication a report containing the Food Standards Committee's recommendations for standards for processed cheese. The committee recommends: (*a*) That processed cheese be defined as cheese which has been heat-treated with or without the use of emulsifying salts, and the fat of which consists entirely of butter fat. Colouring matter may also be added. "Flavoured processed cheese means processed cheese to which a flavouring substance has been added." (*b*) That a minimum butter-fat content of 48% in the dry matter, and a maximum moisture content of 42%, be prescribed for processed cheese; that a minimum butter-fat content of 45% in the dry matter, and a maximum moisture content of 45%, be prescribed for processed cheese of the Gruyère and Emmenthal varieties. (*c*) That a maximum quantity of 3% emulsifying salts be permitted for all types of processed cheese. (*d*) That cheese spread be defined as cheese prepared to spread easily by the addition of one or more milk products, with or without the application of heat. Emulsifying salts, colouring matters, and flavouring substances may be added. "It shall have a minimum content of 45% of butter fat in the dry matter and a maximum content of 48% of moisture." (*e*) That the ingredients of cheese spread be disclosed on the labels in accordance with Article 2 of the Labelling of Food Order (S.R.O., 1946, No. 2169).

Reports of Societies

WORKING CONDITIONS IN HOT AND DEEP MINES

Empire Mining Congress

The recent Empire Mining and Metallurgical Congress at Oxford passed one of its sessions considering the physiological and psychological effects of heat and humidity in deep mines. The discussion was mainly concerned with the mines of South Africa and India, but it was pointed out that the subject was becoming increasingly relevant to British coal-mines. In India mines have reached a depth of 9,300 ft. (2,790 m.), and, although in South Africa there are no mines so far below the surface, leases have been granted which will make mining to 10,000 ft. (3,000 m.) a possibility. In Western Europe a mine of 3,000 ft. (900 m.) would be considered deep, but the subject was important here if recruitment to the mines was to be unhindered by uncomfortable underground conditions.

Dr. A. CAPLAN spoke of the psychological effects seen under conditions of high environmental temperature in the Kolar gold-fields in Bangalore, South India. The miner subjected to high temperatures, he said, suffered from mental fatigue not only during the shift but after his work was over, and in certain individuals this contributed to maladjustment and anxiety and depressive states. The men became apathetic, careless, accident-prone, and ready prey to the agitator. This view was endorsed by the superintendent of the Mysore mine on the Kolar gold-field, Mr. J. K. LINDSAY, who said that the miner of to-day would not put up with the conditions tolerated by his forebears. According to his observation the first symptom of mental fatigue in the mines was a tendency to shout, to pay undue attention to trifling incidents, and to get the work done speedily at all costs. In his experience such mental fatigue lasted longer than physical fatigue, and mental clarity was not recovered until the following day. It had been found in the Kolar gold-field that the miner could work comfortably and efficiently at wet-bulb temperatures up to 83° F. (28.3° C.); even at 85° F. (29.4° C.) the loss of efficiency was slight; it became considerable at 87° F. (30.6° C.), and at 90° F. (32.2° C.) the efficiency was down to about half the normal. One speaker said that he had paid a visit to some German mines at Hamm. When the wet-bulb temperature exceeded 82° F. (27.8° C.) in these mines the length of the shift was automatically reduced, so there was an inducement to the management to keep down working temperatures for the sake of production. Other experts declared that a wet-bulb temperature of 80° F. (26.7° C.) with a dry-bulb temperature of 90–95° F. (32.2–35° C.) and a moderate air velocity made extremely pleasant conditions in a mine, not unlike those of a summer day so far as temperature and air movement were concerned. Figures were given of the cases of heat collapse in the Kolar gold-field since the installation of cooling plants five years ago. During the five years before the plants were started the number of cases of heat collapse was 406, with two deaths; during the last five years the number has been 26, with no death.

Dr. J. S. WEINER, of the Department of Human Anatomy, Oxford, described an experiment at the City Deep mine in Johannesburg which showed that Bantu labourers—not only novices but trained men—although they had spent all their lives in a hot climate, were less able to adapt themselves to conditions in the mine than were well-acclimatized Europeans. One South African speaker said that he had obtained the views of more than 30 experienced European foremen in the Rand mines on the question of acclimatization. The majority of them agreed that acclimatization could be acquired in about 15 days; some considered that it could be acquired in a week. It was their opinion that after one to two weeks' absence from underground work there was a slight loss of acclimatization which was recovered a few days after return, but a significant loss occurred after a month's absence. About half the foremen considered that some acclimatization remained after an absence of three to six months. Cases of heat collapse occurred most frequently among men who were resuming underground work after a short remission. The co-ordination of measures to combat heat and humidity and those to combat dust presented a problem. With water used to suppress dust the wet-bulb temperature might be raised considerably, because the strata were cooled by such a process and not the air. Moreover, as coal was broken up into finer particles more heat from oxidation was generated in the dust, and this could be a serious factor in a deep coal-mine.

Nova et Vetera

ROYAL COLLEGE OF SURGEONS IN IRELAND

An Account of the Schools of Surgery. By J. D. H. Widdess, M.A. (Dublin), L.R.C.P.&S.I. Foreword by William Doolin, F.R.C.S.I. (Pp. 107. 17s. 6d.) Edinburgh: E. and S. Livingstone. 1949.

This entertaining history of the foundation and growth of the Royal College of Surgeons in Ireland and its schools gives a picture of the growth of surgery in Dublin. Surgery there followed the same general lines of development as in London and Edinburgh, with colourful touches added by the Irish temperament. The same progress can be seen from itinerant charlatanry through guilds allied with the barbers and wig-makers to a company and finally to a college.

In 1745, when the London Company of Surgeons received their charter, a society of surgeons existed in Dublin, but no systematic training was available. The foundation of the Royal College of Surgeons in Ireland in 1784, however, preceded that of the Royal College of Surgeons in London by 16 years. The Irish College has from the outset taken a lead in education, and in the first half of the nineteenth century the College held classes and conducted examinations in the preliminary sciences and in medicine as well as surgery. This responsibility was accepted by the English College only within the last quarter of a century. As in London, much of the teaching in anatomy and surgery was undertaken by private schools like the one run by the Hunter brothers in Windmill Street, but in Dublin these flourished until much later, and the last two, the Carmichael and Ledwich Schools, were incorporated in the College in 1889.

There is entertainment as well as interest in this book. In the early years of the Irish College the Dublin poor, having buried their relations with ceremony and celebrated their interment with spirit, took no further interest in the departed. The resurrection men, provided they observed a modicum of decency, were therefore able to supply the anatomists with abundant material—so abundant that the export of cadavers to England was at one time a flourishing trade, and one professor was wont to illustrate his discourses on war surgery by propping a series of subjects round the lecture theatre, firing his revolver at them, and demonstrating the lesions that resulted.

The troubled history of Ireland colours the pages. Then as now one of the chief exports of the country was medical officers for the armed Forces of the Crown. But while many served in British uniform, others were fanatical rebels. William Lawless, professor of anatomy, was expelled from the College in 1799 for treason. He joined Napoleon's army, was wounded at the battle of Dresden, and had his leg amputated by Larrey. Knowing the dangers of hospital gangrene, he mounted his horse at the end of the operation and rode off to Mainz without changing the dressings. This is a colourful book that will interest any student of the history of surgery.

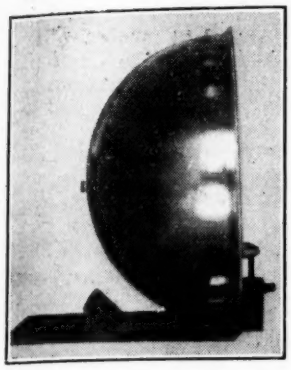
HENEAGE OGILVIE.

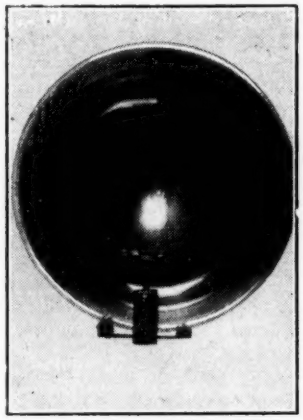
A new international non-governmental body, the main object of which is to co-ordinate international congresses of medical sciences, was created at Brussels in April, 1949. The final establishment of this new organization was the result of much preparatory work carried out by a group of scientists under the joint sponsorship of WHO and Unesco, and it will fill the long-recognized need for a permanent organization to ensure continuity and co-ordination of medical congresses.

Preparations and Appliances

A TRANSPARENT "PERSPEX" PERIMETER

Dr. CECIL M. RUBEN, of London, N.W.3, writes: The perimeter described below is made from a "perspex" half-sphere; the material is colourless, transparent, and about 4 mm. in thickness. The instrument has no movable parts. I have found the chief disadvantage to be the formation of troublesome reflections if care is not taken to place the head of the patient between the source of light and the point of fixation. When the source of light is a window in daylight, or an opalescent globe, so long as the general illumination of the room is good, image formation will not interfere with the test if the above



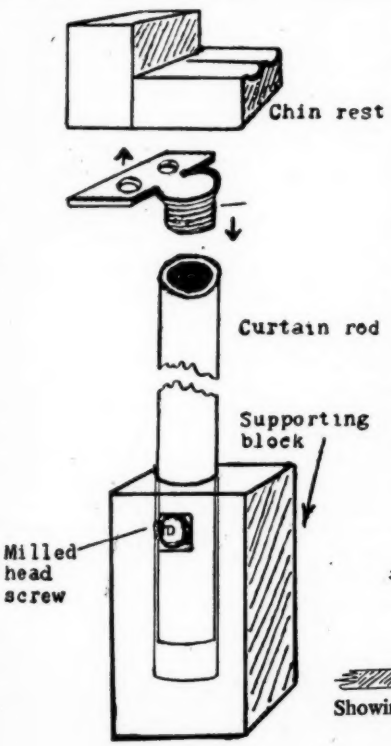


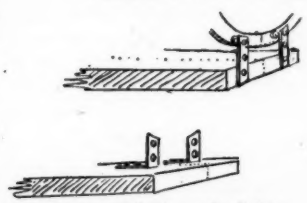
position is obtained and if only *one* source of light is used. The perimeter being transparent, the point of fixation can be placed at any distance. Best results will be obtained with a dull background.

The instrument combines the simplicity and speed of the clinical confrontation test with the accuracy of perimetry. I made the instrument for 30s. The parts required are: (1) Astral dome, ex-R.A.F., made of perspex. I bought mine at one of the stores selling ex-Service equipment for 25s.; it has a radius of 300 mm. (2) Piece of wood 18 by 9 by ½ in. (45 by 22.5 by 1.25 cm.). (3) Two metal right-angled brackets. (4) A piece of metal rod (curtain rod) 5 in. (12.5 cm.) by ½ in. (1.25 cm.) diameter. (5) Curtain-rod fitting. (6) Piece of wood 4 by 2 by 2 in. (10 by 5 by 5 cm.). (7) Black matt paint or black cloth. The dome has to be marked by scratch lines indicating the meridians 15 degrees apart and the concentric circles at 10-degree intervals. The circumferences at the periphery will be $2\pi r = 3\frac{1}{7} \times 600$ mm. $= 1{,}885\frac{5}{7}$ mm. Therefore the distance between the peripheral points will be:

$$\frac{1{,}885\frac{5}{7}}{24} = 7.8 \text{ cm.}$$

These intervals are marked in ink on the peripheral flange and opposite points are joined with scratch lines made with a needle; care must be taken that all lines pass through the centre. (A piece of pliable cardboard about ½ in. wide by half the circumference in length is suitable as a ruler.)





Showing methods of fixing brackets.

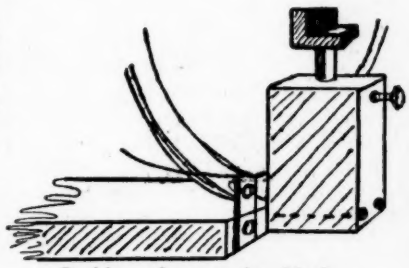
The concentric markings are made with a large pair of mathematical dividers, one end being placed at the centre, the other swept around the inside surface of the dome. The distance between the circles is equivalent to

$$\frac{\pi r}{18} = 5.25 \text{ cm.}$$

The base is now taken and the metal brackets are fitted at one end equidistant from the midline; the spacing must be exact and they must be over 4 in. apart. The vertical meridian of the perimeter must be held in alignment with the central line of the base, and in this position two marks are made on the flange opposite the holes in the supporting brackets. Holes are drilled through at these marks and the dome fixed into position by nut and screw (¼ by ½ in. (0.3 by 1.25 cm.) long). It is best if the flange just rests on the base. Surplus bracket projecting into the perimeter is sawn off.

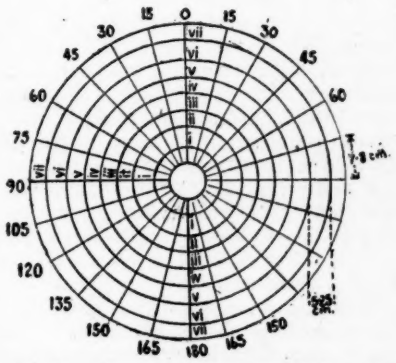
The chin rest is made from two pieces of wood 4 by ½ by 1 in. (10 by 1.25 by 2.5 cm.), and the chin depressions are filed out. This rest is fixed to the curtain rod by the support shown, and the supporting block has a hole ½ in. in diameter drilled through its centre vertically. The fixing screw must be improvised from a nut and screw with a milled head, the nut being sunk into the wood in line with the shaft and near the top.

The centre of fixation can be made from anything suitable. My dome had a hole at the centre and my fixation point is a screw-head painted white held in position by a nut and a black rubber tap-washer. The supporting block can be screwed to the end of the base or into its top surface according to the position of the right-angled brackets. The flange is marked in indian ink with numerals ¼ in. high indicating the angle of the meridians according to the recording charts used. The concentric circles can be indicated by markings i, ii, iii, iv, v, vi, vii, corresponding to 10→80 degrees; they need not be higher than 2 mm. and only along four meridians. The base is painted black or covered with cloth. It is best to employ targets as used with screen scotometry; with a pencil in one hand and a chart held in the same hand as the target rod, or vice versa, recording is more rapid.



Position of supporting block.

Another refinement is to scratch the normal limits of the field on the perimeter—a continuous line for the right field and a dotted line for the left field. This will enable the less experienced and occasional perimetrist to note departures from the normal without making a detailed recording. It is best to have the central 10-degree area bare of all scratch lines so as to assist fixation. The perspex can be polished with ordinary metal-polish and a soft cloth.



Showing the grid to be scratched on to the dome.

Correspondence

Training College for Medical Teachers

SIR,—The reading of your interesting educational number (September 3) stimulates me to write about an idea which I have thought and talked about but never aired in print—the training of medical teachers, at present non-existent. It appears that even elementary teachers are trained and exercised not only in the material they present but in the method of its presentation. They are taught not only what but how to teach, and are helped in the latter by trial and helpful criticism. As regards clinical medicine, undoubtedly the most difficult subject to teach and impart, no training is available, and teaching ability is a somewhat minor consideration in appointments to a teaching hospital. Some few are wonderful teachers by innate ability, others are inferior and often inaudible, and probably all could be improved by training and criticism when they are young.

I seriously suggest the need for a school for medical teachers, chosen naturally from the registrar type. Here for two or three months the best young medical brains in the country would be thrown together. They would have courses of elocution, psychology, methods of teaching, logic, and sociology; lecture to each other, be taught how to speak, present slides, and make reasoned presentations; and be criticized by their teachers and themselves in all they did. They would be taught to teach and how to think in the scientific method as far as possible. They would be endlessly stimulated by the endless talking of shop, with variants of tennis, music, beer, or what have you. What a glorious chance for themselves and the future of medicine.

Such an institution must presumably be set up near a good medical library and near abundant clinical material. Presumably the students might be paid by the Health Service at their established grading, but some organization would have to initiate such a scheme. I feel that the Nuffield Foundation could spend its money in no better way. And who are to be the leaders, the teachers of the future teachers? Difficult to find, but essential for success. The writers in your recent educational number show that the medical profession is not lacking in persons of the right calibre.—I am, etc.,

London, W.1. R. D. LAWRENCE.

Distinction Awards

SIR,—Successive Governments, Coalition, Conservative, and Labour, have had this in common, that they all wished to introduce a national health service. In these circumstances it would be difficult for any profession to resist the wish of the people. It would plainly be impossible if that profession were not unanimous. There have been two alternatives open to those who practise medicine. Either we can guide and help the Government of the day to set up such a service, or we can hold aloof, leaving it to the Ministry of Health to plan such a service unaided. The Royal College of Physicians has repeatedly affirmed their faith that co-operation would be for the good of the country and for the good of the profession.

When the remuneration of consultants was first under consideration it seemed probable that professorial salaries of that time would be taken as a maximum. At this juncture Lord Moran proposed in the House of Lords that the whole subject should be investigated by a special committee. The terms eventually proposed by the Spens Consultants Committee, and accepted by the Government, have justified the wisdom of this step. Indeed, these terms have been criticized by the Treasury and by other professions as unduly generous. There is good reason to believe that the laymen on the Spens Consultants Committee, who were in a majority, would not have agreed to these terms if seniority alone had been the deciding factor. They were attracted by the provision of an incentive which they felt would contribute to the efficiency of the consultant service.

One of your correspondents asks pertinently, "What is the alternative?" The answer is that there is none. If the consultants do not want merit awards I am sure that the Treasury will meet their wishes with alacrity. Let us be under no illusion. I speak from the book when I say that there will be no substitute. The money for these awards will not be available for any other purpose, such as an all-round addition to basic salaries. It is well that the profession should know where responsibility lies if the considerable sum of money allocated for these awards is lost to consultants. Is Dr. F. M. R. Walshe (August 13, p. 383) speaking for consultants, and in particular is he speaking for the younger generation who have to work the service? The Royal College of Physicians decided unanimously to give any assistance they could to the Awards Committee. The Royal College of Surgeons have been equally constructive. The same action has come from many quarters, including Scotland.

I do not believe that the system of awards for merit is either undesirable in theory or unworkable in practice. The whole system of remuneration appears to me to be a sensible compromise between the claims of seniority and the claims of merit. Moreover, professional distinction will be decided in the future more by the profession and less by the laity. There are of course many analogies for monetary awards: the prestige of the Nobel prize-winners, for example, is not obviously impaired by the fact that a committee picks out certain men for considerable monetary reward.

The element of novelty in these awards is perhaps the explanation of such criticism as has been voiced in your columns. But the response of regional boards and teaching hospitals to Lord Moran's appeal for help and advice has already made it plain that the great majority of consultants intend to do what they can to ensure an equitable distribution of these awards. And I am confident that those medical committees which have not already met will take the same constructive line.—I am, etc.,

London, S.W.1. H. E. A. BOLDERO.

SIR,—I should like to add my support to those who have joined their voices to Dr. F. M. R. Walshe's admirable protest (August 13, p. 383) against the distinction awards scheme for specialists. In this, as in other matters, what is important is that not only must justice be done, it must plainly be seen to be done. Any arrangement which makes it necessary for part of the profession, no matter how eminent, to decide on the fortunes of their fellows is bound to give rise in some to bitter suspicions of injustice and nepotism, whether or not such suspicions have any foundation in fact. If awards retained the relative rarity of an Honours List recognition they would fall only to those whose eminence was universally admitted. But when every third or fourth man gets a prize his colleagues may well have reason for envy.

Having said this, we must in common fairness avoid the use of such phrases as "Nothing could be more calculated, etc.," not to mention the "Nazi" methods of Dr. Katharine Lloyd-Williams (August 27, p. 485) and the "Divide and rule" of Dr. C. C. Beatty (September 3, p. 545). For it is clear that nobody has deliberately set out to produce the probable results I describe, and the awards scheme, so far from being the Machiavellian plot of the Ministry of Health, is part and parcel of the methods advocated by the independent Spens Committee, which included several eminent consultants, for bringing specialists' salaries to the proper level. The Government gave a pledge in advance to accept the Spens report, and they might rightly be criticized if they had refused to do so. It is unjust now to attribute to them the unpleasant consequences of part of this report. We might too, if we wished, regard the proposals as a laudable attempt—though an attempt fraught with the usual consequences of good intentions—at retaining incentive and initiative in a nationalized service.

I believe that there is some evidence that the Government would be glad to be relieved of the odious responsibility of fulfilling its promise in this respect. But we could only expect

the scheme to be abandoned at the unanimous request of the profession, as expressed through the Association and the joint Consultants Committee. Would such a request be unanimous? Would those whose position or connexions gave them reason to regard themselves as likely recipients of an award vote in favour of abandoning the scheme? I for one would willingly live on the basic salary scale for specialists rather than take my chance in a haphazard hand-out of prizes which was bound to make some of my friends uneasily triumphant and some miserably disgruntled.

I imagine that the democratic machinery exists by which it could become the Association's official policy in negotiating to dispense with the award proposals, either entirely or in favour of some generally acceptable alternative. It is not part of my business here to state what alternatives are available. Dr. Walshe himself in the past has supported the right to purely destructive criticism where it is justified, and nowhere was it more justified, or more easily directed, than here.—I am, etc.,

London, W.1. DAVID LE VAY.

Posts, Not Individuals

SIR,—The confusions and anomalies up and down the country in the allocation of salary-carrying titles are due to one cardinal error—the attaching of titles to individuals and not to posts. This statement is based on actual experience of the work of assessment and appointments committees during the last six months. The same error has set the Distinction Awards Committee a task which it cannot perform equitably.

The allocation of titles to posts might properly be based upon types of hospital, of which there are four. (1) The country or cottage hospital. The staff here is open; every general practitioner of the neighbourhood has the right of use. The appropriate title of the members of the staff is general practitioner; the salary is that of their general practice. (2) The town hospital. The staff is selected. The appropriate title for all these selected members is specialist; the salary that of the Spens scale. (3) The area hospital, or hospital group; otherwise styled district or key hospital. The staff here is also selected. The appropriate title for its members is consultant; the salary scale a percentage (perhaps 20%) above the Spens scale. (4) The regional hospital group. In addition to the services provided by the area hospital group, this group provides special services (neurosurgical, etc.) and teaching. The proper title for the staff is consultant and teacher; the salary that of the consultant with additions for teaching duties.

This definition of the regional hospital group assumes the merging of the teaching hospitals with others of the regional centre. Such a merging would be nothing but the correction of the administrative error of separating the teaching hospital from the general scheme of providing for the sick—a correction which some boards of governors are making voluntarily. As an error, it exemplifies the putting of second things first, instead of adjusting secondary duties to the primary duty.

Of details I mention only one. In the special hospitals (mental, chest) the senior member of the staff and his deputy should be styled consultant, the other members specialists or specialists in training. As for distinction awards, promotion takes their place. I have not touched upon the subject of liaison between one grade of hospital and others, for its general lines can be readily drawn.—I am, etc.,

Faringdon, Berks. K. W. MONSARRAT.

Mosquito Eradication

SIR,—I have read with great interest the leading article on mosquito eradication (July 23, p. 222). There is one conclusion which emerges obviously from the various experiments with residual insecticides which have been reported so far from various parts of the world: the introduction of D.D.T. and other similar residual insecticides has provided us with new and truly wonderful tools for the control of malaria, but these insecticides, as with all the methods of control formerly known, to be effective and economically feasible must be applied intelligently—i.e., with a full knowledge of local epidemiological conditions and with very special reference to the bionomics of the local vector or vectors. Conclusions drawn from experiments conducted in Cyprus, Sardinia, or British Guiana have a significance which is strictly limited to the local vector and to local oecology. Generalizations in the malariological field are no more warranted to-day than they were yesterday, before the introduction of residual insecticides.

While in the past control methods were principally based on a full knowledge of the breeding habits of mosquitoes, residual spraying techniques, even with the most effective insecticides, require a very thorough understanding of the feeding, biting, and resting habits of the adult insects. Anthropophilic and domestic species are specifically vulnerable to attack by residual techniques, and eradication becomes possible. Mosquitoes which bite in the open and do not enter houses, on the contrary, cannot be affected by residual spraying methods. Species with eclectic feeding habits, which attack both man and animals, will continue to be abundant even in spite of residual treatment.

In the neotropical region *A. darlingi* and *Aëdes aegypti* are strictly anthropophilic and domestic; both have been successfully eradicated in the settled areas of British Guiana by residual methods only. This has been accomplished under a wide range of environmental conditions, including the coastal plantation belt and localities in the forest, savannah, and mountainous areas of the interior. This range of conditions is fairly typical of those prevailing over a huge portion of tropical South America, where *A. darlingi* is the main malaria vector. It was the knowledge of the selective biting habits of *A. darlingi* which enabled us to make a successful plea for the release of D.D.T. to British Guiana in 1944, when this insecticide was still on the secret list and strictly reserved to military use. *A. darlingi* can be taken as the prototype of mosquitoes susceptible to 100% control by residual D.D.T. house-spraying.

At the other end of the scale we find *A. bellator*, an efficient carrier in the cocoa-growing districts of the interior of Trinidad; this species breeds in the bromelias infesting the immortelle shade trees of the cocoa plantations. It bites in the open and by day; it never enters houses. This mosquito can be expected to be as refractory to residual spraying methods as it is to conventional hydrological control.

In between these two extremes we have species which are only partly domestic and anthropo-zoophilic in their biting habits. With such species, of which the notorious vector *A. albimanus* and *A. aquasalis* are examples, residual methods can give only partial results. The transmission of malaria will probably be reduced by the elimination of individuals which actually enter houses to attack man, but the total species population will hardly be affected. In British Guiana residual methods, limited to house-spraying, have had no effect whatsoever on the population of *A. aquasalis*.

In this colony we have achieved localized eradication of both *Aëdes aegypti* and *A. darlingi* (the latter, it should be noted, is an autochthonous forest species) under continental conditions. The possibility of reinvasion of the area which is to-day free from these mosquitoes is an obvious possibility if the periodical application of D.D.T. is not continued indefinitely. Yet even here, with an adequate knowledge of local topographical oecology, it will be possible to whittle down spraying operations to a number of strategic localities dominating the probable routes of reinvasion. Spraying operations have already been closed down on certain coastal sections, where the situation is being closely watched with an intensification of check surveys. We are taking advantage of such natural barriers as wide rivers, brackish marshes, and belts of acid soils with surface waters unsuitable for *A. darlingi* production. Elsewhere mountain ranges or stretches of open wind-swept savannah could be utilized as natural barriers. Even under continental conditions natural obstacles can frequently be found and exploited, but here again the definition of such obstacles depends on the complete knowledge of the biology of the local vectors and a thorough understanding of local environmental conditions.—I am, etc.,

Georgetown, British Guiana. G. GIGLIOLI.

Carcinoma of the Gall-bladder

SIR,—The annotation (August 13, p. 376) suggests that a decision for or against cholecystectomy should be influenced by the possibility of carcinoma developing in a gall-bladder containing stones. As I have recently contributed to a textbook an exactly opposite view, I should like to justify myself.

When we advise an operation with an immediate mortality of at least 1–2% in order to avoid some possible disaster in the remote future, our decision is based on probabilities and we must try to make a rough arithmetical estimate. The first difficulty is to find suitable data. Statistics of gall-bladder surgery tend to be misleading, because the patients attending a large and famous hospital are a selected and unrepresentative sample. Standardized mortality rates are based on the whole population and avoid fallacies of selection; but they are open to serious criticism because of unavoidable mistakes in death certification, especially in the older age groups. The least objectional data are thus male and female death rates at ages 45–65, and several independent lines of argument suggest that the following figures from the Registrar-General's occupational mortality returns (based on the 1931 census) showing annual death rates per million living are approximately accurate:

	Ages 45–55		Ages 55–65	
	Men	Married Women	Men	Married Women
All causes of death combined	11,141	7,658	23,552	16,431
All forms of cancer combined	1,606	2,024	4,685	4,012
Gall-stones, cholecystitis, etc.	37	91	111	218
Carcinoma of the gall-bladder	10	20	42	82

If we accept your citation from Graham[1] that 8–10% of all carcinomata start in the gall-bladder we are almost driven to assume that about 90% of patients who die from gall-bladder carcinoma are falsely certified as dying from carcinoma of the stomach or colon, and that in reality the gall-bladder is one of the commonest sites of a primary cancer. Even Kirshbaum's[2] figure of 3% would create difficulty. The Registrar-General's figures fit in far better with clinical and necropsy experience.

The next question is the incidence of gall-stones at different ages in the general population. Here we are compelled to accept necropsy figures, but these are so extensive and agree so well that they should be fairly reliable. At ages over 45 at least 5% of men and 10% of women carry stones. Most authors put the figures considerably higher, but as a result of modern austerity the incidence is possibly falling.

The statistical argument now runs as follows. It is not unlikely that the association between gall-stones and carcinoma is in part due to mucosal changes producing stones, and not vice versa. But let us assume that every gall-bladder carcinoma is the result of stones and that the whole incidence of the disease falls on the group with stones. Then, in order to get the incidence of gall-bladder carcinoma in patients with stones, we must multiply the rates just given by 20 for men and by 10 for women. We can then deduce that the probability of a man dying between 45 and 55 is 1.1131 in 10 if there is no risk of gall-bladder cancer, and 1.1331 in 10 if there is a risk of gall-bladder cancer. The biggest difference occurs in women aged 55–65, where the respective risks are 1.6349 in 10 and 1.7169 in 10. Various incalculable factors might alter these risks slightly in either direction, but all my assumptions have tended to exaggerate the benefit to be gained from cholecystectomy.

Surely the reward is incommensurate with the immediate risk. The immediate risk is 1–2%, and the benefit between the ages 45 and 65 is less than 1%. A better statistical case could be made out for universal appendicectomy or gastrectomy. Life cannot be lived on the basis of sacrificing our working years for an intricate actuarial calculation of an increased expectation of life as an old-age pensioner. The decision in favour of cholecystectomy must be based on a clinical judgment of more immediate benefits.—I am, etc.,

London, E.1. DENYS A. JENNINGS.

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The M.R.C.P.

SIR,—The annotation on the M.R.C.P. (August 6, p. 327) suggests that "the decision of the College is one the consequences of which it does not seem to have thought out to the end," and goes on to predict a lowering both of the status and the standard of the examination. While no one who happens already to have achieved the membership can regard lowering of its status or standards as anything but catastrophic, there is room for doubt whether the writer of the annotation is not suffering from a lack of prescience similar to that which he criticizes in the committee when he expresses the hope that in two years' time "the College will consider the possibility of holding, instead of the M.R.C.P., a primary examination, possibly in conjunction with the Royal College of Surgeons, as a preliminary to a final examination for the F.R.C.P., say four or five years after qualification."

For were this suggestion to be adopted what would be the status of the pre-1949—or even the pre-1951—Members? At present no Member can become a Fellow by examination: and I venture to predict that Members who had obtained their M.R.C.P. under the conditions which have so far prevailed would consider themselves utterly betrayed were the F.R.C.P. to be made obtainable by examination while the M.R.C.P. became obsolete or depreciated.

The procedure which would in fact become necessary if the F.R.C.P. were at some future date to be made obtainable by an examination of a standard comparable to that of the present M.R.C.P. would be to elevate all existing holders of the M.R.C.P. to the Fellowship. This would of course rob the F.R.C.P. of the special distinction which at present attaches to it as an individual honour, in that while the M.R.C.P. and the F.R.C.S. are strictly comparable, there exists no counterpart to the F.R.C.P. in the officially designated hierarchy of the Royal College of Surgeons at all. To maintain this difference in designation appears to have been the agreed policy of the Comitia to date.

To remark that "the method adopted by the Royal College of Surgeons appears to be more rational and fair" is a comment which, whether considered reasonable or not, is utterly irrelevant in the present context; for the terms of reference of the committee did not include a consideration of the desirability of equating the F.R.C.P. with the F.R.C.S., thereby lowering the status of the F.R.C.P. and abolishing the M.R.C.P. altogether. Whether this is or is not in fact desirable is beside the point as long as it is the status, standards, and function of the M.R.C.P. which are under consideration.—I am, etc.,

Boston, Mass. DAVID STAFFORD-CLARK.

Structure and Function of Muscle

SIR,—I would be glad of an opportunity to correct two misunderstandings in the report (July 16, p. 160) of a paper given to the Section of Anatomy at the Harrogate meeting of the British Medical Association.

The pattern of re-innervation of human voluntary muscle varies with the nature of the lesion in the main nerve trunk and the severity of atrophic changes in the muscle itself. Thus, after a favourable lesion such as axonotmesis, the degree of re-innervation may be normal and maturation is of a high degree, although abnormal branching is seen at the motor end-plates. Where there is scar tissue at the site of injury of the nerve some of the axons are obstructed and others may be misdirected. In such cases the intramuscular nerve trunks may contain both empty Schwann tubes and others containing nerve fibres in varying stages of maturation. Cutaneous sensory fibres fail to make functional reconnexions with the muscle. If atrophic changes in the muscle are advanced and re-innervation is delayed, the axons are seen to have left the terminal Schwann tubes, and they pass across muscle fibres in an attempt to form new connexions. If the atrophic changes are irreversible the highest degree of re-innervation is of no avail.

Fibrillation action potentials are characteristic of denervated muscle fibres—they are wholly independent of voluntary effort. One of the early signs of re-innervation of muscle is the return of motor-unit action potentials. In cases which go on to

successful recovery these motor-unit action potentials may precede probable voluntary contraction by 10 to 20 days in cases of pure axonotmesis. In cases where the nerve has been sutured or there is a lesion in continuity with considerable intraneural scar they may precede voluntary contractions by several weeks or even two to three months. The appearance of a few motor-unit action potentials is no guarantee of useful recovery; where such recovery is taking place successive electromyographic examinations of the muscle show an increasing number of motor-unit action potentials.—I am, etc.,

London, W.C.1. RUTH E. M. BOWDEN.

Headaches after Spinal Analgesia

SIR,—During recent discussions with anaesthetists and surgeons in this country and in America, the problem of the relief of post-spinal headaches has arisen several times. A measure which has been consistently effective since 1930 has been that of the intravenous injection of 20 ml. of 30% saline. It may aggravate the condition for 20 minutes, but at the end of half an hour the cephalalgia disappears and the ability to read and to concentrate is restored. On one or two occasions during the past 20 years it has been necessary to repeat the injection the following day, and also to combine it with placing the patient in the high Trendelenburg position for half an hour, but it has always succeeded.

It has proved equally effective in persistent post-traumatic headaches and also in those occasional ones following a diagnostic lumbar puncture. I have seen no ill effects from it beyond soreness at the point of injection when some of the salt has been inserted paravenously. Miss Joan Walker (*Brit. J. Surg.*, 1936, **24**, 105) wrote on the effectiveness of hypertonic saline in raising a fallen blood pressure in spinal anaesthesia, and in a personal communication she told me that in the patients in which it had been used the incidence of post-spinal headaches was reduced.

The effectiveness of hypertonic saline for post-spinal headaches was suggested by its efficacy in the persistent cephalalgia of syphilitic basal meningitis. This remedy for insistent headache is so dependable and simple that it merits being widely known.—I am, etc.,

London, W.1. HAROLD DODD.

Silicone Pan Glazes in Bread Production

SIR,—We are concerning ourselves increasingly with the study of the possible effects of absorption and ingestion of new products of chemical origin finding their way into the baking industry. It has recently been pointed out[1] that a food which may be regarded as wholesome should make its expected contributions to human nutrition and be clean and free not only from harmful bacteria but also from substances which might be classed as chemical contaminants. The increasing number of new technological aids which are, and have been, developed for use in the growth, storage, and processing of food make it necessary for individual examination of such new products, particularly if ingested, for both acute and chronic toxicity. It is equally important to demonstrate in certain cases that usage of new materials, of which the silicones are an example, is unlikely to lead to their absorption by the product being manufactured. In such cases the information required is simpler, inasmuch as analytical procedure will suffice without recourse to the lengthy physiological examination which is necessary to demonstrate the harmlessness of materials which are absorbed and consequently ingested.

In the particular instance of silicone pan glaze it has already been shown[2] on experimental animals that this substance is very low in chronic oral toxicity. It is our view, however, that analytical evidence in a case of this type removes some of the uncertainties in translating results on experimental animals into terms of human metabolism and that problems generally of this nature require investigation by as many diverse techniques as possible.

As a result of our earlier work on the use of mineral oils in baking,[3,4] on which we based recommendations to the industry, the advent of the Mineral Oil in Food Order[5] has made the tolerances we suggested the legal limits beyond which mineral oils must not be present in foods as a result of processing. It is clear, therefore, that to attain these limits the baking industry must exercise the greatest care in using mineral oils for tin greasing or machinery lubrication, and any step which might be advised to replace the former operation would be an advantage provided the harmless nature of the replacement can be demonstrated.

For some time we have been examining the use of silicones as water-repellent glazes for bread-baking tins, these materials having been used in America and latterly on a restricted scale in this country to eliminate entirely the use of tin greases whether of edible or mineral character. The silicones are polymers containing silicon, oxygen, and alkyl radicles (R) and may be regarded as complex molecules possessing thermostable properties of the type

When dissolved in a solvent such as solvent naphtha (the inflammable nature of which probably precludes their use by many smaller bakeries unless some central distributing and processing organization can be created), these silicone solutions can be painted, sprayed, or otherwise distributed on a baking-tin and, after drying to remove the inflammable solvent, are rendered hard by baking at the usual temperature. In this way a thin durable glaze comprising a synthetic resin is created on the tin which can withstand repeated use approximately 200 times without renewal or carbonization of the coating.

We have investigated carefully the possible absorption of the resin by bread baked in silicone-coated tins and have been unable to detect by chemical means any increase in the proportion of silicon present in the crust of the loaves so obtained, irrespective of the method of application of the silicone solution to the surface of the tin. The method used was to compare the silicon content of the crust of a loaf baked in a silicone-treated tin with the content of the crust of a loaf prepared from the same dough baked in a greased tin—the crusts being treated chemically to convert any silicone present to silica, followed by colorimetric determination of the total silica in each case. In a series of comparisons no result was obtained which indicated a higher final silica content in the case of loaves baked in tins coated with the silicone resin. It should of course be borne in mind that bread naturally contains a small amount of combined silicon, hence the use of the comparative method outlined.

We have also investigated the loss in weight of a normal silicone film during a series of baking experiments, and the average loss per baking with very slight deviation was 0.0000006 g. per sq. cm., or 0.00045 g. per 2-lb. loaf tin. Even if one assumes that the entire loss is due to absorption by the loaf—which the previous experiment described indicates as unlikely—this loss would only represent a final proportion of approximately 0.00005% of silicone in the loaf, or less than 0.5 parts per million of silicon. It is possible that, as the silicone glaze is fairly easily scratched by sharp metal, stacking of the tins between bakings will cause slight removal of the coating.

In view of the data now put forward, and the earlier toxicological findings reported,[2] we do not consider that silicone pan glazes in bread production involve any potential harmful effect on the consumer and that the very small amount of silicon naturally present in bread is not materially increased by this process.—We are, etc.,

The British Baking Industries Research Association, Chorleywood, Herts, and the Royal Technical College, Glasgow. J. B. M. COPPOCK. H. HULSE. A. URIE.

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3 *British Medical Journal*, 1948, **2**, 401.
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Gravitational Ulcers of the Leg

SIR,—Dr. S. T. Anning's excellent article on the aetiology of gravitational ulcers of the leg (August 27, p. 458) calls attention to a fact which is not commonly recognized—the importance of thrombosis of the deep veins as a cause of these common and disabling lesions.

I cannot help commenting on the extremely high incidence (86.6%) of deep thrombosis in Dr. Anning's cases, for, while I agree whole-heartedly that deep thrombosis is a very common causal agent, I am sure that in general it is not nearly so much

to blame as Dr. Anning's figures would suggest. Certainly in a large varicose-vein clinic attached to my service a relatively high percentage of leg ulcers are due to simple varicose veins and considerably less than half are associated with deep thrombosis. Probably the explanation is that as a dermatologist Dr. Anning does not see the majority of the varicose ulcers which are quickly and satisfactorily dealt with in the surgical clinics, while on the other hand a great many of the cases with deep thrombosis gravitate eventually to the skin clinics.

There are undoubtedly thousands of cases of gravitational ulcers of the legs receiving "dermatological" treatment both in skin clinics and from practitioners, and it is refreshing to find a dermatologist calling attention to the fact that these ulcers are a problem in hydraulics rather than dermatology, and that infection plays little or no part in their production. It is time that the profession learnt that ointments and lotions are at best useless in the treatment of these ulcers. I cannot remember seeing a gravitational ulcer during the last few years that had not been having penicillin applied as an ointment or given by injection. All too often the ointment produced a severe skin reaction.

It is good to find Dr. Anning adding his experience to that of Boyd and Robertson regarding the risk of deep thrombosis when varicose veins are injected at the same time as they are ligated at the sapheno-femoral junction. I know that many authorities on varicose veins, such as Dickson Wright and Dodd, still advocate this method. I agree that severe complications are uncommon, and I confess that for years I myself taught and wrote advising simultaneous ligation and injection—in 25 years I remember only one personal case when deep thrombosis resulted—but as a consultant to the Navy during and since the war and to the Ministry of Pensions I have seen a distressingly large number of cases where gross oedema, ulceration, etc., followed this practice.

The treatment of deep thrombosis and its complications has until recently been distressingly futile. Undoubtedly prevention is the best treatment, and the introduction of heparin and dicoumarol and a proper realization of the causes of the condition should help us to reduce the numbers of cases developing it. There will, however, always be a great many patients who will only be seen too late and who will already have developed oedema, pain, and ulceration. Surely we cannot be content to offer these patients nothing but elastic support. The problem is one not for the varicose-vein or the skin clinic alone but for them in conjunction with the radiologist and surgeon, for undoubtedly the surgical techniques of Bauer and Linton and Hardy are giving results which more than justify further consideration.—I am, etc.,

Liverpool, 1. J. B. OLDHAM.

SIR,—Dr. S. T. Anning (August 27, p. 458) concludes from a study of 270 "unselected patients" that treatment of varicose superficial veins is harmful more often than not. I should like to suggest that a high degree of selection has been achieved, as he has collected a number of cases who have had sclerosing injections without benefit, the remainder being cases of "white leg," which are obviously unsuitable for varicose-vein injection. Dr. Anning gives no figures concerning ulcers healed by injections.

My own personal impression is that the incidence of gravitational ulcer has decreased since 1929 by at least 80%. At that time no practice was complete without three or four chronic leg ulcers, whereas now ulcers are relatively rare. Some of this improvement is due to better understanding of nutrition. I have for instance seen an indolent ulcer heal after vitamin-C saturation with no other treatment, but most have required some sclerosing injections, occasionally helped by a subcutaneous ligation in our own practice.

The only chronic leg ulcers in our practice now are the really difficult cases. If the deep veins are thrombosed and the superficial veins varicose and therefore not functioning in the erect posture, the leg is perilously close to gangrene, and tight bandaging is not as a rule tolerated by the patient. There is no cure for these cases except amputation or indefinite rest in bed. They are unusual compared to the cases of ulcus cruris which heal after a few injections, or occasionally after only one. I feel that Dr. Anning has been seeing the failures and should study the successes before coming to a conclusion.—I am, etc.,

Shipley, Yorks. H. S. RUSSELL.

SIR,—The subject of gravitational ulcers is treated rather ungratefully by your annotator (August 27, p. 480)—"The many books and papers on this subject in the last 20 years have not been very fruitful"—and more realistically by Dr. S. T. Anning (p. 458). Dr. Anning deals with only one aspect of the problem—no doubt a deep-seated one—but one has to point out that, in the words of an eminent doctor, "On the black and marigolded mud the moorhen's footsteps print." (*On the Hill*, by John Masefield.)

The condition of the deep veins is important and is easy to neglect, but this problem is bound up with what one might term the "soil," and the "soil" includes "dirt," trauma, malnutrition, associated diseases, stagnation of circulation, autophytic influences, tissue inertia, and some other unknown factors. In addition to the "soil" one must consider the "seed," in other words the factor of infection. This may be staphylococcal and/or streptococcal—the "synergistic infective gangrene of skin" described by Meleney—the Vincent's organisms associated with tropical ulcer, *Corynebacterium diphtheriae*, and some others.

In addition to the "soil" and the "seed" the day-to-day and seasonal alterations in "climate" or weather have an important influence, and bodily fatigue or overwork and exhaustion must be considered. The anatomical distribution of small arteries to the superficial areas of the leg between knee and ankle, particularly the ring a few inches above the ankle, have a bearing on the formation and healing of these gravitational ulcers.

It is not the knowledge or treatment of these conditions that is defective—as hinted in your annotation—it is merely the practical application in general practice (and I do not blame general practitioners) which is defective. A short account of the factors involved in the evolution of these ulcers was published in 1945 (*Trans. R. Soc. Trop. Med. Hyg.*, 1945, **38**, 259), and a method of treatment suggested, which proved not unfruitful.—I am, etc.,

Epping, Essex. FRANK MARSH.

Significance of Convulsions in Infancy

SIR,—The article by Drs. P. W. Nathan and P. M. Ransford (August 20, p. 421) presents some convincing statistics, indicating that convulsions occurring in infancy are likely to be the precursor of epilepsy. But surely the suggestion that any child having convulsions should, without careful individual study, be submitted forthwith to anticonvulsant medication is rather drastic. Repeated convulsions, it is generally agreed, are much more likely to be epileptic than those occurring singly, but, even when they are multiple, family history, possible precipitants, and the type of attack should first be considered.

It is, perhaps, not quite fair to attribute to Peterman the view that convulsions within the first two years are of no serious significance. In a later and more comprehensive communication[1] he finds birth trauma by far the commonest cause of convulsions, single or multiple, occurring in the first month of life. During the succeeding five months convulsions associated with acute infections take first place, with infantile tetany and birth trauma as less frequent causes. From 6 months to 3 years febrile convulsions still head the list, with idiopathic epilepsy, birth trauma, and tetany a good way behind. A large number of less common causes are, of course, cited. The outlook, *qua* fits, for the cases of idiopathic epilepsy and birth trauma needs no comment, but Peterman is now inclined to think that acute infection may precipitate fits only in children with a low convulsive threshold, itself evidence of a hereditary predisposition, and this he has confirmed in some cases by the E.E.G.

Margaret Lennox[2] has made a more detailed study of febrile convulsions arising in early childhood. Boys are twice as commonly affected as girls, and a family history of convulsions (not necessarily epilepsy) is found in nearly half the cases. Among

those who subsequently developed epilepsy the initial convulsion was more severe, and the incidence of birth trauma and of positive family history much higher. The clinical picture is confirmed throughout by the E.E.G., and Margaret Lennox suggests that children who have febrile convulsions should have an E.E.G. record within a week of the attack, a month later, and again at the age of 3. When indicated by clinical and E.E.G. findings anticonvulsant drugs might usefully be given up to the end of the third year. This would appear a sound policy to aim at for all cases of convulsions in early life.

It is commonly stated that the incidence of infantile convulsions is very much less than it was a generation or two ago. Is there any published evidence of this decline? There is, so far as I know, no reason to suspect any increase or decrease in the incidence of idiopathic epilepsy, and if the majority of early convulsions belong to that category we must assume that some fit-precipitants have disappeared. A fall in acute infections is unlikely, but it may be that dietary deficiencies have been made good, or that more intelligent and careful supervision of feeding has lessened alimentary upsets. Anyway, here would be a field for exploration, of especial interest, perhaps, to those who are investigating the role of metabolic factors in epilepsy.—I am, etc.,

Purley, Surrey. J. TYLOR FOX.

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SIR,—Surely Drs. P. W. Nathan and P. M. Ransford (August 20, p. 421) have reached their conclusions too easily and swiftly. They quote a series of known epileptics attending hospital and a smaller group of ordinary out-patients for a contrast. The former group was almost bound to contain a number of "items" which had some sort of fits in infancy, and the latter group is far too small, and memories even of parents are likely to be too unreliable.

I do not know what the incidence of infantile convulsions is at the present date, but I do remember that 40 years ago, when I was in general practice near here, the onset of the ice-cream season was a time when I expected to be called out of my bed fairly regularly to give hot baths, etc., to many a baby or young child who had been indulged. There were also many cases in which the exanthemata were ushered in by a convulsion. These cases never developed epilepsy, and indeed when I meet many of them now they introduce me to some buxom daughter or capable son as the man who "saved their lives" by a hot bath. Should I have kept these youngsters under sedatives (bromides, because we had no phenobarbitone) as Drs. Nathan and Ransford suggest?—I am, etc.,

Brixham, Devon. CECIL B. F. TIVY.

SIR,—May I be permitted to make some observations upon the article by Drs. P. W. Nathan and P. M. Ransford (August 20, p. 421), in which they confirm the finding of a higher incidence of infantile convulsions in epileptics than that found in the general population. In the brief space available to them there was obviously no question of a general review of the literature, but it appears to me that brevity in this case has created rather a false impression. To say without further qualification that a convulsion within the first two years of life indicates that the child is an epileptic is likely to lead to an unnecessarily gloomy prognosis that may well be hotly challenged by those with experience of convulsions in childhood.

Their figures are not remarkably different from those reported by Patrick and Levy,[1] who found 20% of infantile convulsions in 500 epileptic children and only 4% in 752 unselected controls; nor from those of Burr,[2] who found a history of convulsions in infancy in 15% of a large series of epileptics. It is difficult, however, to see how these facts alone warrant the conclusion "that convulsions within the first two years of life are to be taken as manifestations of epilepsy" and that recurrence is to be expected. Surely all that they do indicate is the well-known fact that epilepsy very frequently begins in early life and often in infancy.

The only accurate way to determine the prognosis of infantile convulsions is to follow up for an adequate period a series of infants who have had observed convulsions and see whether in fact they have any more. A most searching investigation on these lines has been published by Thom.[3] In 395 children with infantile convulsions only 12% developed epilepsy, while the incidence of epilepsy in 8,000 unselected children was 1%. From this it is fair to conclude that there is an increased chance of epilepsy in those with infantile convulsions as a whole, but, while 88% of these children remained free from further fits during the period of observation, it is scarcely legitimate to dub them all epileptic, let alone to treat them as such.

The whole argument depends obviously upon what one means by epilepsy. I have taken it that the authors have used the term in the usual sense of a chronic convulsive disorder characterized by recurrent convulsions and the strong likelihood of subsequent mental deterioration. This concept is convenient and time-honoured, even if aetiologically unsound. Nevertheless, taking this definition, it is certainly not true that most children who have an isolated convulsion at the onset of an acute infection are "epileptic." On the other hand, the convulsion appearing "out of the blue" and unaccompanied by acute illness is very much more suspect, while repeated convulsions should always be regarded as potentially epileptic.—I am, etc.,

Glasgow. ROBERT A. SHANKS.

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1 *J. Amer. med. Ass.* 1924, **82**, 375.
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3 *Amer. J. Psychiat.*, 1942, **98**, 574.

*** In addition to the above letters and that from Professor R. S. Illingworth and Dr. S. A. Doxiadis (September 3, p. 547), letters criticizing the paper "Significance of Convulsions in Infancy," varying in detail but similar in substance, have been received from Dr. C. Elaine Field (London), Dr. N. Malleson (Ipswich), Dr. A. Lewis (London), Dr. A. A. McInnes (Wellingborough), Dr. D. Pyke (London), Dr. N. F. Elliott Burrows (London), Dr. J. B. Metcalfe (London), Dr. S. G. Siddle (Malton), and Dr. J. C. R. Morgan (Llantrisant).—ED., *B.M.J.*

Tuberculosis in European Voluntary Workers

SIR,—In the course of routine clinical duties among the population in an extensive and fairly representative area of the West Riding of Yorkshire I have been astonished by the number of cases of pulmonary tuberculosis which have been discovered among European voluntary workers who have immigrated to England during the past few years under the Ministry of Labour schemes.

It may well be that this finding is a mere impression on my part and one which may not be substantiated by detailed statistical investigation. Yet it is rather alarming to note that some at least of such new recruits to British industry have never had an *x*-ray examination prior to their acceptance for employment in this country, and others who claim to have had such an examination have demonstrable pulmonary infiltrations when examined within a few months of arrival in Yorkshire.

Clearly there is no room in this matter for political prejudice or parochial nationalism, but it must be borne in mind that one tuberculous E.V.W. may easily saddle the Exchequer with a bill for over £1,000 for his treatment and for the maintenance of his family during his stay in an institution and subsequent rehabilitation. The whole situation is even more perplexing when it is recalled that both the Canadian and South African Governments insist on the most rigorous health qualifications, including the production of a chest radiograph by all prospective British immigrants. Apart from the financial aspect of this problem, the further danger of introducing a new and perhaps more virulent strain of the tubercle bacillus among the indigenous population of this country may prove to be something more than mere academic speculation (see Mr. Walter Elliot's paper in the *Journal* of August 6, p. 297).

Finally, while conceding the need for additional sources of manpower in the current export drive, every effort should be made by the Ministry of Labour or the appropriate Government agency to introduce the highest possible health standards among all European workers recruited for British industry.—I am, etc.,

Halifax. BERTRAM MANN.

Torsion of Normal Fallopian Tube

SIR,—May I record a further case of torsion of an apparently normal Fallopian tube?

In June, 1947, I was called to see a woman of 48 (para 2) with severe lower abdominal pain, this being her fourth attack of similar pain in twelve months. Each attack had lasted about twelve hours. On examination, a tender swelling, estimated to be 1½ in. (3.75 cm.) in length, was palpable in the left fornix. A diagnosis of twisted ovarian cyst was made, and at operation the left tube was found to be swollen, black, and twisted on its mesosalpinx. The ovary was not involved, and there was no obvious reason for the torsion. The other tube and both ovaries were normal.

—I am, etc.,

Southampton. RAYMOND PURVIS.

Growth of Foetal Head

SIR,—I have read the letter on this subject by Dr. A. G. Murray (August 13, p. 387). Like the late R. E. Roberts, I have estimated foetal maturity on the assumption that the foetal skull grows at a constant rate during the last month of pregnancy. I have probably made over a thousand of these examinations since Reece[1] described his method in 1935, and my impression that this method is of definite value has gained strength through successive years—particularly so in the last six hundred cases, in which the proved accuracy of the vertical shift technique[2] has contributed to the precise measurement of Reece's greatest circular section. Reece based his calculations of foetal maturity on the work of Calkin, who showed that the diameters of the head are proportional to the length of the foetus.

Proof of growth in the last month is difficult if cephalometric results are not accepted as reliable evidence. Clinical measurements immediately after birth are apt to be upset by moulding. If the foetal head does not grow during the last month cephalometry at the 36th and 40th weeks would give similar results. This is not so in my experience. The greatest circular section will have increased by about four-tenths of an inch (1 cm.).—I am, etc.,

Reading. PAUL CAVE.

REFERENCES

1 *Proc. R. Soc. Med.*, 1935, **28**, 489.
2 *British Medical Journal*, 1943, **2**, 196.

Haemorrhage into the Spermatic Cord

SIR,—The following case was erroneously diagnosed as a strangulated hernia by two independent doctors of experience.

On April 26, 1949, a boy aged 13 was playing football and, while running, he became aware of a slight pain in the left groin not associated with any injury at all. During the next five minutes the pain increased in intensity until it became fairly severe but not excruciating. He cannot remember whether he ran about or remained still during the time when the pain became more severe. At this time he noticed that a lump had developed in the groin.

After an hour the pain diminished gradually and he was able to sleep that night, but was aware of the pain on awaking next morning. His doctor was called and, finding a tender irreducible lump with no impulse on coughing, he diagnosed a strangulated hernia and sent the patient into hospital with a letter which read, "Though not appearing typically like a hernia I think it is one." This diagnosis was substantiated by the doctor who saw the boy on admission to hospital.

At operation on the next day (April 28) the lump was found to be due to swelling of the spermatic cord, which was black in colour throughout its length. Torsion of the testicle was suspected and the tunica vaginalis opened, but the testicle and epididymis were seen to be quite normal. The coverings of the spermatic cord were then divided and the entire cord was found to be infiltrated with blood clot. This was gently swabbed away with dry gauze, but the bleeding point had evidently sealed and was not discovered. There was no hernial sac. The wound healed by primary union and recovery was uneventful.

Evidently this condition can simulate a hernia on clinical examination and can cause the surgeon to suspect a torsion of the testicle at operation. It should be borne in mind in the differential diagnosis of surgical emergencies of the inguinal region.—I am, etc.,

Boston, Lincs. CHARLES MACLAY.

Stress Incontinence in the Female

SIR,—I have followed the correspondence on this subject with interest. So far none of your correspondents has pointed out that this condition may be a neurotic manifestation simply and solely, due to neither anatomical nor organic neurological causes. To attempt to cure such a case by any form of operation would be as likely to be followed by permanent cure as an attempt by a thoracic surgeon to cure the air swallower by slinging up the oesophagus.

Non-realization of this may lead to one of the most worthwhile operative procedures, the cure of stress incontinence, coming into unwarranted disrepute.—I am, etc.,

East Boldon, Co. Durham. TERENCE G. ROBINSON.

Dermographia

SIR,—A case of dermographia came under my care recently, and the following particulars may interest your readers.

The patient, a nurse, consulted me on December 16, 1948, suffering from dermographia which she had had for several months. Her skin was extremely sensitive to the touch—a thumb-nail drawn lightly over the surface causing a weal to come up almost immediately. The weal took about five minutes to come up, during which time intense pain was experienced, but this passed off as soon as the weal was fully formed. Such simple movements as crossing her legs, combing her hair, or even lying in bed caused these weals to come up. In consequence of this she was becoming very debilitated and nervous. She found hot baths relieved the pain, although the friction of the towel while drying herself again aggravated her condition.

She had previously had desensitization tests, which proved negative. This was followed by a course of peptones and later by typhoid shock treatment, neither of which gave her any relief. She was then put on a milk diet with calcium injections and hydrochloric acid by mouth, without result. While under this treatment in hospital she lost a stone (6.3 kg.) in weight. After a period of four months there was no improvement. One of her fingers became infected, and she was treated with penicillin. The result of this was a further aggravation of her condition. It was at this stage that she consulted me.

A radiograph of her chest was negative. The only possible focus of infection which could be found were her tonsils, which were enlarged and pitted but which had been passed as satisfactory during the time she had been in hospital. With a view to improving her general health and sedating her nerves I decided to try to build up her general condition by a simple tonic containing lime, phosphorus, and iron, phenobarbitone gr. ½ (32 mg.) t.d.s., and general ultra-violet-light treatment. She had six general ultra-violet-light treatments before the end of the year, and these then stopped for five weeks. She received them again every other day in February for nearly four weeks, and she had a further three treatments in the middle of March. On April 1 she reported that she still had a very little dermographia, but there was no further burning and her general condition had improved considerably.

On further consultation with a nose-and-throat specialist her tonsils were removed as being a possible focus of infection, and early in May she had returned to full duty in hospital (being a sister in charge of a ward) completely relieved of her symptoms.

This case is interesting, demonstrating as it does the remarkable effect of ultra-violet light on this condition, which had resisted various forms of treatment. In addition it is important in such cases to make sure that any doubtful focus of infection is eradicated.—I am, etc.,

Christchurch, New Zealand. W. GORDON RICH.

Production of Dental Caries

SIR,—I was most interested in the article by Dr. P. Pincus on the production of dental caries (August 13, p. 358), and I found his logical reasoning as he took it step by step, smashing the lactic acid theory on the way, quite fascinating. While appreciating the considerable research he has done in this con-

nexion, it is difficult to agree with his final conclusion, in which he points out that certain Gram-negative bacilli in the mouth are the cause of caries in that they release sulphatase, which acts on one of the organic compounds of dentine and enamel proteins, liberating sulphuric acid, which attacks the calcium salts.

At first sight the cause of caries seems to have been found, but on second consideration the actual cause seems as obscure as ever, and what Dr. Pincus has described is the probable chain of events after the cause has been set in motion. What the cause is, Dr. Pincus admits earlier in his article, is unknown, for he there states that "sulphatase has so far not attacked intact dentine or enamel protein," and then goes on to say that "before the sulphatase can act on the tooth it would seem that initial hydrolysis of the protein (of the enamel and dentine) must take place; it is not known at present how this initial reaction occurs."

When we discover what causes this initial hydrolysis of enamel and dentine proteins we shall have discovered the cause of caries. Until then it is erroneous to ascribe the cause to the presence of certain Gram-negative bacilli in the mouth, as these only exercise their effect after the process of decay has started.—I am, etc.,

Slough, Bucks. H. TUDOR EDMUNDS.

Death after Neostigmine Injection

SIR,—The note by Professor R. R. Macintosh (May 14, p. 852) and the letter from Dr. J. Clutton-Brock (June 4, p. 1007) on the subject of sudden death following the injection of neostigmine recall the details of the following case.

The patient was a deeply jaundiced baby of 7 weeks, admitted to hospital with a provisional diagnosis of congenital atresia of the bile ducts. At 1 a.m. on April 22, 1949, it was said to have "frothed at the mouth and gone cold" in the ward. It recovered from this attack after excess mucus was removed by sucking. An intravenous saline drip was set up before operation at 2 p.m. the same day, and continued throughout. Induction was by means of open-mask ether, followed by a dose of 0.7 mg. *d*-tubocurarine (body weight of the child being 6 lb. 7½ oz.=2.9 kg.) injected into the tubing of the drip. After 20 minutes a further dose of 0.2 mg. was given and anaesthesia continued with ether and oxygen. Relaxation was adequate, and the operation lasted one and a half hours. Respiration and pulse were satisfactory throughout.

At the completion of operation, as the child was being moved about for the application of the bandage, 0.25 mg. of "prostigmin" and 1/300 gr. (0.22 mg.) of atropine were injected into the tubing. The patient collapsed forthwith, the heart-beat being inaudible and the respirations absent. The usual remedial measures of artificial respiration, inflation with oxygen, and the injection of 0.5 ml. of nikethamide were of no avail. Post-mortem examination revealed no abnormalities other than the congenital one at the site of operation.—I am, etc.,

Sydney. MARIE HILL.

An Antibiotic of Wide Range

SIR,—Your leading article (August 27, p. 477) on the valuable therapeutic properties of "aureomycin" states that the drug is now being used on an enormous scale in the U.S.A., and ends with the sentence: "The task of those who have to decide how many precious dollars to spend on this new antibiotic and how to distribute such supplies as reach this country can be no easy one."

The inference appears to be that the amount of the drug available in this country is limited to some extent by the dollars available for its purchase. If this inference is correct, then it seems a most opportune time to express the hope that the flow of this and other life-saving drugs will be made as immune from the effects of sterling-dollar crises as is the two-way flow of medical ideas and information.—I am, etc.,

Rostrevor, Co. Down. J. A. FISHER.

POINTS FROM LETTERS

Distinction Awards

Dr. H. V. DEAKIN (London, N.W.3) writes: I hasten to congratulate Dr. F. M. R. Walshe on his excellent letter (August 13, p. 383) under the heading "Distinction Awards." I look upon Dr. Walshe as one of the few sane men still to be found in our profession, and one after my own heart in that he fears no man, minister, or president. I still have a letter written by him and termed "The Commonplace Mind," which was published in the *Journal* of February 28, 1948 (p. 407). No more devastating and dignified answer to the present Minister of Health was ever penned. Let us hope with Dr. Walshe that if nothing else can kill this irrational affair stone dead a sense of the ridiculous will put an end to the Distinction Awards Committee.

"Ockham's Razor"

Dr. R. E. REWELL (London, N.W.8) writes: Professor A. P. Thomson (July 30, p. 243, and August 6, p. 300) does not appear to recognize "Ockham's Razor" as a fundamental principle of logic, and as the reason why more than one disease process should not be invoked to account for any multitude of symptoms and signs presented by a patient unless it is necessary to do so. The whole trouble would appear to be what is meant by "necessary," and Professor Thomson does well to protest against the dead hand of tradition passed on by a succession of registrars who have never heard of so out-of-date a teacher as William of Ockham (or Occam). He is more recent than Aristotle, as the *Dictionary of National Biography* gives the date of his death as "? 1349," but both of them would join with Galen in condemning any uncritical perpetuation of their ideas. Even to-day medical men do know the names at least of the Roman and the Greek, but their own countryman has sunk into complete darkness. For the sake of any of the uneducated who may still be interested, here is Ockham's "razor": ***Entia non sunt multiplicanda praeter necessitatem.***

A Population Policy

Dr. JOHN A. MCCLUSKIE (Perth, Western Australia) writes: Your leading article on a population policy (June 25, p. 1127) largely endorses the findings of the Royal Commission. Yet there is one question the Commission has not answered. You state, "We must rely, given reasonable social conditions, upon instinctive desires for a family. . . . But the 'reasonable social conditions' are fundamental. Broadly they fall under two headings: (1) financial assistance or relief and (2) services for the special benefit of children and mothers." If this is true, why have the best-off families the smallest number of children? The answer is that except in the case of extremely strong personalities instinctive desires for a family are incompatible with modern material comforts. . . . The fact that the birth rate rises with the extenuating conditions of war is good evidence that some factor other than "reasonable social conditions" is "fundamental." Anyone who cannot follow the inhibiting effect of fear and comfort can at least realize that the poor have the least fear of loss and, as a result, the biggest families.

Psychogenic Rheumatism

Dr. W. A. O'CONNOR (Kingswinford, Staffs) writes: While it may be admitted that the paper on psychogenic rheumatism by Drs. William Tegner, Desmond O'Neill, and Anna Kaldegg (July 23, p. 201) presents certain dangers inherent in the splitting-up of all hitherto accepted classifications, it cannot be but a step in the right direction. To the general class of reader it may well appear to be a revolutionary step; to the newly orientated psychiatrist, to whom psychodynamics is an accepted concept, the subject matter is nothing startling. He will feel grateful for this contribution, even though he may feel, as I do, that we have entered only upon the first stages of an intensely interesting pilgrimage towards a wider understanding of human psychosomatic aberrations. The authors of this paper have shown the true pioneering spirit. So have those who were instrumental in helping them and to whom they have acknowledged their indebtedness. And I, for one, praise the Editor of the *Journal* for having courageously set the cat amongst the pigeons. . . .

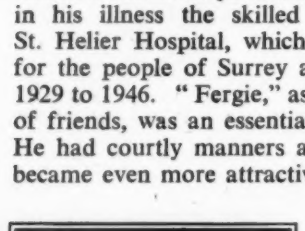
Haematemesis Due to Aneurysm

Dr. FR. KLEIN (Bratislava, Czechoslovakia) writes: With reference to Dr. G. M. Barrett's report (August 6, p. 319) on a case of haematemesis following intraduodenal rupture of aneurysm, I described, together with A. Bárdos, a similar case about a year ago (*Schweiz. Z. Path. Bact.*, 1948, **11**, 387). In this an atherosclerotic pseudo-aneurysm of the aorta ruptured into the descending part of the duodenum (2 cm. beyond Vater's papilla) in a man aged 61. No signs of syphilis were found.

Obituary

JAMES FERGUSON, C.B.E., M.B., D.P.H.

Dr. James Ferguson died on August 27 after a painful illness borne with quiet courage. As was fitting, he received in his illness the skilled medical and nursing care of St. Helier Hospital, which is a monument to his services for the people of Surrey as County Medical Officer from 1929 to 1946. "Fergie," as he was known to a vast number of friends, was an essentially lovable and gracious person. He had courtly manners and a handsome presence which became even more attractive as he grew older.



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James Ferguson was born in Muckamore, County Antrim, in 1879, and received his education at the Royal Academical Institution and Queen's College, Belfast. As an undergraduate he was president of the Belfast University Students' Union. He obtained, first of all, an honours degree in classics at his university with the intention of entering the higher Civil Service. Throughout his life he retained his intense love of the classics and deepened his appreciation of literature. Cultured in the widest sense, his many reports on public health affairs, meticulously considered and models of literary art, bore the hallmark of a cultured mind. But his career was not to be in the Civil Service, for illness supervened and he did not pursue that course. He turned to medicine and graduated in 1908, later adopting public health as his specialty. It was a happy decision, for he lived to adorn the specialty of his choice. But in whatever branch of medicine he had practised Ferguson would have been successful, for not only did he acquire the highest academic distinction and a quiet philosophic approach to his problems but he possessed in large measure the qualities of human understanding and sympathy for others. They endeared him to all with whom he came in contact; indeed, it can be said with complete assurance that he had no enemies.

Perhaps his most effective work was done in the committee room and through his multifarious reports on all aspects of the public health service of the Surrey County Council, to which he came after a distinguished career as Chief Assistant County M.O.H. for Lancashire, where he served under Dr. J. J. Butterworth. For these high public health offices he had undergone excellent preliminary training through house appointments at his teaching hospital, followed by several years in general practice in Rochdale under a great general practitioner, Dr. Bateman. Ferguson also held an appointment for several years in a mental hospital in Gloucestershire, where he laid the foundation of his considerable general knowledge of mental hospital administration, which played such a great part in the building up of the Surrey County Council's combined hospital service in which the mental hospitals and the general hospitals and sanatoria all came under the county medical officer as their administrative chief. Under his guidance this system was to prove an efficient prototype of the close association now being attempted under the National Health Service between mental hospital and general hospital services.

In committee and through his written reports he exercised great influence, not alone because of his wide knowledge and high intellectual ability, which, with his characteristic modesty, he always underestimated, but also because of the thoroughness with which he prepared his work and his elegant and scholarly English. His delightful Ulster accent added to the charm of his expositions. He had a marvellous memory, and always recalled accurately the surnames and initials of everyone he met in the course of business. Though unsurpassed in skill in debate in the comparative privacy of the committee room and in the preparation of written reports, he was inhibited, by a diffidence and shyness which were attractive features of his character, from showing to the best advantage when speaking in public.

Ferguson's visible monument is St. Helier Hospital. But even more important to those who worked under him (and the numbers of those now holding high positions, both medical and lay, in the public health service who have been assistants to Dr. Ferguson is legion) is that for 18 years, as a natural consequence of his personal character and also his deliberate policy, he maintained in the Surrey County Council's public health service a harmonious team. He had the necessary attribute in a chief of being content to see his assistants given their full share of credit for the work of the department. Reference must be made to his steadiness and courage, both moral and physical, throughout the difficult war years, when, moreover, he insisted on taking his full and heavy share of night duty. It is impossible to estimate how much his conduct did to keep his staff unperturbed so far as possible during the vicissitudes of the years between 1939 and 1945 when so much was laid on local government departments. He felt bitterly the loss of what should have been the years of progress between 1938 and 1946, but such feelings did not turn him aside from his immediate duty to see that the work of his department and its share towards the war effort went on unimpeded. He had indeed a natural and simple pride because he had the opportunity to play such an important part in maintaining the essential services of Surrey county throughout these war years. Few who knew him as the embodiment of physical and mental vigour, working all the hours that a man could possibly work, realized that before the 1914–18 war he had a long and serious illness, from which he made a complete recovery but on account of which he was refused, to his great humiliation and despite numerous attempts, a commission in the R.A.M.C. in 1914.

The main energies of James Ferguson were always devoted to the service of his employing authority, but, busy man though he was, he managed to fit in a great amount of work for the Society of Medical Officers of Health, the Association of County Medical Officers, the Royal Sanitary Institute, and the British Medical Association, in each of which he held a very distinguished place. He was a member of the departmental committee on partially sighted children between 1932 and 1934, and a member of the committee dealing with the cost of hospitals and other public buildings between 1933 and 1938. The latter committee played no small part in turning his thoughts in the latter period of his office so much to hospital affairs, but he maintained also the closest association with the school medical and child-welfare services and with the work of his colleagues, the district medical officers of health in Surrey, with whom he held the happiest relationships.—W.G.P.

Sir Andrew Davidson writes: The passing of James Ferguson, affectionately known as Ferguson of Surrey, removes another of the great medical officers of health of the past generation. My friendship with him extends over

20 years, strengthening with the passing of time; and with it came an ever-increasing appreciation of his influence in public health. So intuitive was his selection of staff, so inspiring and encouraging was his leadership, and so practically sound was the training he gave them that many of his young men now occupy high positions in the public health service. He was loved and respected by them all, and later they often turned to him for guidance and help that was never refused. Ferguson came to Surrey from Lancashire in 1929 to take over from Professor E. W. Hope, of Liverpool, who had been acting county medical officer for some nine months. Those were difficult days in the history of public health in Surrey. Two main influences conspired to create new problems—the transfer of Poor Law functions to the County Council with the consequent need for reorganizing the hospital service, and the rapidly increasing population with the need to develop the existing health services. Ferguson threw himself whole-heartedly into the solution of these difficulties; and, with his capacity for reducing the most abstruse problem to its simplest form, the background of his experience in Lancashire, his unsparing energy, and the confidence which an enlightened county council had in him, the county health services were slowly built up to be equal to the best in the country. Ferguson's reputation as a leader in public health was established and the inevitable followed. He was a first choice for innumerable committees on health affairs; indeed, no such committee was complete, particularly those concerned with hospitals, without the name of Ferguson of Surrey. A catalogue of the committees on which he gave such valuable advice and guidance would be too lengthy to include here. But his help was also sought by examining bodies for the D.P.H.: he was examiner for London and Manchester Universities and for the English Conjoint Board.

One project to which Ferguson gave much effort was the development of the health services of the great L.C.C. housing estate at St. Helier. The provision of a first-class school health service, a health centre for the local preventive services, and a new hospital were only parts of that scheme. In particular, he was justly proud of St. Helier Hospital. Tribute has been paid in naming the nurses' home of that hospital "Ferguson House." He was proud, too, when he was made an Honorary Physician to the King in 1941; he felt it was one of the highest honours in the profession—and it was richly deserved. Later he was to receive further recognition in 1946, when he was created a C.B.E. But his greatest satisfaction came from the knowledge that he had been the architect of the efficient and extensive health services of the county which he served so well. So highly was Ferguson's knowledge, experience, and administrative ability appreciated that he was not allowed to retire at the end of his service in Surrey. He was offered a temporary appointment as a principal medical officer at the Ministry of Health: he accepted and, with the highest commendation from those whom he served there, he continued to give of his best. Unfortunately, the last two years of his life were darkened by an insidious illness which he bore, with fortitude, to the end. Few, if any, knew that he was ill; he suffered in silence lest he should worry his friends. When I saw him two weeks before the end it was clearly evident that he was resigned to the inevitable. Indeed, his "Good-bye" was an emotional moment not readily forgotten.

The passing of James Ferguson will leave a gap in many places where his friendship was cherished, and his wide circle of friends will offer to Mrs. Ferguson, his daughter, Doreen, and the two grandchildren their deepest sympathy in their irreparable loss.

Dr. F. Hall writes: News of the death of James Ferguson was received with great regret by his friends and former colleagues in Lancashire, where he spent the earlier part of his public health career. From 1920 until his appointment as county medical officer for Surrey he occupied the post of chief assistant medical officer to the Lancashire County Council, a period during which the health services of that county were actively developed. Intellectually brilliant and endowed with a clear and constructive mind, Ferguson exercised an important influence on this process and helped to lay the sound foundations upon which the services were built. Those of us who were in the service at that time will long remember not only his friendly and helpful counsel but also his thoughtful and discerning views upon major social and health problems. Large numbers of the more unfortunate members of the community he served, particularly the blind and crippled children, also owe him a debt of gratitude for the thorough and sympathetic manner in which he exercised his administrative functions in arranging for their welfare. The public health services and the medical profession have lost an honoured and valued member, one who at all times maintained the highest ethical standards of medicine in all its varied relations.

W. T. WARWICK, M.B., F.R.C.S.

Sir Gordon Gordon-Taylor writes: Some years ago I wrote of a distinguished Australian surgeon that he was "a man of few words, a flair for diagnosis, and a sharp knife": these words would not inaptly describe my old friend and colleague, Turner Warwick, with the substitution of the terms "careful" and "deliberate" for "sharp." Warwick, whose obituary notice was printed in the *Journal* of September 3 (p. 549), was never an architect of talk, not that he was unready to take part in any discussion that was for the benefit of his patient or on a subject upon which he entertained strong views, but he was not publicly disputatious, and I imagine that he felt the strain each time he was compelled to participate in open debate. His diagnostic flair was extraordinary: he was the first, or at least one of the first, to make the diagnosis of a ruptured oesophagus; he tentatively formulated the startling diagnosis of actinomycosis of the rectum in a patient of the writer's, subsequently confirming its accuracy by demonstrating the streptothrix fungus on numerous occasions before the patient's death; he unerringly diagnosed a haemorrhage into an intrathoracic goitre in a colleague, when all others in consultation took the most sinister view of the case; it is even alleged that he suspected the rare affection which terminated his own life.

His work and outlook bore the impress of his distinguished senior colleague, William Sampson Handley, and this contact, together with the years of nurture in the Bland-Sutton Institute of Pathology, perhaps inculcated in him a livelier Lucretian interest in the nature and cause of things than in the technical correction or ablation of human affections and ills, perchance sustained by Cromwell's hope: "To be a seeker is to be of the best sect next to a Finder, and such an one shall every faithful, humble seeker be at the end."

He was the "whitest" man that ever lived, "four-square," of transparent honesty, completely devoid of self-seeking, unsparing of effort on behalf of others. Perhaps the affection in which Warwick was held may be summed up in words used of the old St. George's surgeon, Sir Prescott Hewett, who also owned a Doncaster background: "Few men were more beloved by those who were connected with him in practice, whether as pupils or patients, for he was a man 'who would not merely scorn

a base action, but with whom anything base would be inconceivable.'" The idea of any panegyric would have been abhorrent to a nature like Turner Warwick's, but I believe that he would have liked a senior colleague to say of him that throughout life he always played the game. He did.

Dr. WINIFRED PEACEY, who died in April last, was an outstanding figure in the West of England. After studying at Oxford and the London School of Medicine for Women she qualified in 1921. Her father was an Anglican canon, and she was the only Catholic in her family. Two of her sisters became Anglican nuns and several of her brothers became Anglican clergymen. After holding a house appointment she joined the Congregation of the Daughters of the Cross and was appointed to their convent at St. Michael's Hospital, Hayle, Cornwall, in 1925. From then until her death Sister Marie Theresa, as she became, worked unceasingly. During her long term of office as medical superintendent the facilities of the hospital were extended and it became more and more an important link in the chain of hospitals in that area. Sister Marie Theresa became one of the best-known and most dearly loved doctors in the district. The hospital, at first staffed by general practitioners in the neighbourhood, grew under her guidance, and over the last ten years treated nearly all the emergency cases from the surrounding districts of Hayle, St. Ives, and the rural area covering the wild Cornish coast and countryside down to the Lizard and Penzance. Sister Marie Theresa, apart from acting as superintendent, was also responsible for radiography and for most of the anaesthetics administered. Three or four years ago she estimated that she had given 16,000 anaesthetics for all types of cases with only one death on the table. She participated fully in the religious life of the convent, gave lectures to the nurses, and supervised the busy physiotherapy out-patient department. Although a nun, she spoke her mind on all occasions, and it was her forthright character which endeared her to those who understood her and appreciated her great qualities. In common with the other members of her sisterhood she scarcely ever left the hospital or convent grounds, but nevertheless she knew every family in the district and conducted the business affairs of the hospital with precision and impartiality. Thanks to her firm and fair management of the hospital there was never any friction among the medical staff of specialists and practitioners, and her ruling was always accepted as final. During the 10 years which I spent in surgical work at the hospital I came more and more to depend on her sound judgment in clinical matters. Over many long hours of operating by day or night one came to rely on her impassive moral support from the "top of the table" and to bow to her cryptic remarks when surgical zeal began to outrun discretion. Sister Marie Theresa was never disturbed by the most irritable surgeon or by the most unreasonable and exacting patient. Few doctors have devoted themselves more whole-heartedly to their profession and looked less for reward or recognition. Her long illness failed to dim her spirit, and she continued to work until the spread of metastases prevented her from walking. It is the greatest satisfaction to all who knew her that she lived to see her hospital saved from State ownership, concerning which she had strong views seldom heard, I imagine, from the lips of one who had chosen the convent for her life's work.—E. C. A.

Dr. GWILYM JAMES, of Aberystwyth, died suddenly on June 24. The son of a sea captain of Aberystwyth, Gwilym James first attempted to follow his father's profession, and he served for a period as apprentice in a sailing ship. Later, however, he studied medicine at St. John's College, Cambridge, and at University College Hospital, where he qualified in 1911. He was a house-surgeon at the Queen's Hospital for Children, Bethnal Green, and also held resident appointments at the Royal Northern Hospital. He settled in general practice in Llanelly in partnership with Dr. Samuel Williams. Here over many years Dr. James won the esteem and affection of his patients by his outstanding ability and his self-sacrificing devotion to his work. He served as a captain, R.A.M.C., with the 2nd Railway Construction Section of the Royal Engineers throughout the 1914–18 war. At Llanelly he was in practice from 1919–43, and he was also honorary consulting surgeon to the Llanelly General Hospital. Ill health compelled his retirement six years ago, and since then he had been living at Aberystwyth, where he renewed many old friendships.

Dr. ARTHUR CARVETH JOHNSON died on June 28 at the age of 63. He was born in West Norwood, London, of Cornish ancestry, and was educated at the Merchant Taylors' School, where he won a scholarship to Downing College, Cambridge, and to St. Thomas's Hospital. He graduated in 1913, and after holding house appointments at St. Thomas's and at the Brompton Hospital he joined the Welsh National Memorial Association for Tuberculosis. He was at first responsible for the districts of Brecon and Radnor, and was transferred to Newport in 1917. Dr. Johnson played rugby for his school and for his hospital. He was a well-known breeder, exhibitor, and judge of bull-terriers, and was a life-member of the Bull-terrier Club. He was at one time chairman of the Newport Canine Society and president of the Newport, Devon, and Cornwall Society. A keep photographer, he was a founder member of the Newport Camera Club, and was its president when he died. At the age of 21 Dr. Johnson was initiated a Freemason, and at the time of his death he was provincial grand senior warden for the province of South Wales, Eastern Division. He was a member of the Newport Medical Society, and he had been in charge of the tuberculosis services for practically the whole of Monmouthshire for many years. He was considered to be an authority on his subject, and his opinion was valued throughout Wales. Dr. Johnson was twice married, and he is survived by a widow and three children.—J. T. R.-E.

Dr. ALEXANDER SCOTT died at his home in Sileby, Leicestershire, on August 16 at the early age of 50. A student of St. Andrews, he graduated M.B., Ch.B. in 1928 and held resident house appointments at the Dundee Royal Infirmary. He had been deputy medical superintendent of Baguley Sanatorium and an assistant tuberculosis officer in Sheffield.

E. K. M. writes: Dr. Scott came to Leicester as senior tuberculosis officer in 1945. His experience of his subject was great, but it is more of his character as a man of which I would write. Following, as he did, a man who had given the last thirty years of his professional life to the work of the local tuberculosis clinic was not particularly easy, but Scott soon endeared himself to the staff and even more especially to his patients. He was a man of great courage and full of life to a remarkable degree. It may be said that he had a zest for living, everything—his profession, his garden, his bee-keeping—his very special hobbies—was so intensely interesting to him. His death was marked by more than one letter in the local press from former patients expressing their lifelong gratitude for the words of cheerful hope which he had been able to give them. Scott leaves behind him a widow and four young children.

Dr. JAMES ANDREW GIBSON died on August 19 at his home in Lancaster. A student of Edinburgh University, he graduated M.B., C.M. in 1895, proceeding M.D. in 1900. After being in general practice at Kendal, he came to Lancaster in 1898. In 1908 he joined the staff of the Royal Lancaster Infirmary, and was in charge of the electro-medical department. He was largely responsible in those early years for the introduction of the first *x*-ray unit to be installed there. He was appointed honorary medical officer to the infirmary in 1911, and was a member of the general committee from that time onwards. Dr. Gibson took a large share in the planning of the original extension of the hospital buildings, and he was elected president of the Royal Infirmary in 1927 and 1928, and again in 1942. He was chairman of the house committee for many years, both before and after his retirement from general practice, and was chairman of the medical committee from 1931 to 1938. He was elected honorary consulting physician in 1939, and he acted as chairman of the local medical war committee during the recent war. Over the past 50 years, while he lived in Lancaster, Dr. Gibson built up a large and flourishing general practice, and for many years was in partnership with Alderman P. F. Mannix. He was much beloved by all his patients, and with

his quiet and assured manner he was a great comfort to many who sought his help. To a few of his more intimate associates his generosity and kindness to the poor and needy were well known. By his professional colleagues he was respected and admired, and his wise counsel and unhurried, unbiased judgment in controversial matters was of inestimable value in the administration of hospital affairs. His colleagues all regretted that during his latter years failing health prevented him from continuing to guide the affairs of the infirmary whose welfare and smooth running were always his first and most important interest. His loss is a great one to all those who knew him, and his memory will be cherished. He was a man of sterling quality, unimpeachable integrity, and a loyal and beloved friend.

Medico-Legal

PARTIAL INTERCOURSE AS CRUELTY

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

Cruelty for divorce purposes is nowhere defined by statute, but the accepted traditional definition is, briefly, conduct endangering or threatening the spouse's life or health. The idea has been gradually clarified by successive decisions of the courts, but each case is decided on its own facts. One of the most recent of these decisions[1] is useful in showing one of the boundaries of legal cruelty and also one of the possible remedies where a spouse suffers from refusal of complete sexual intercourse.

A husband, almost from the outset of the married life, performed partial intercourse by coitus interruptus in spite of the repeated protests of his wife and of his own knowledge that his conduct was increasingly injurious to her bodily and mental health. He abstained for varying periods, and after these had partial intercourse on occasions. On each of these occasions the wife genuinely hoped and believed that the intercourse would be complete and that she could bear a child. Each time she was frustrated, disappointed, and depressed, and her nervous system was disturbed, with the result that her health, both bodily and mental, suffered increasingly, for she keenly desired to raise a family and believed that her husband did also.

At last, losing hope of the marriage, she petitioned the court for nullity on the ground of the husband's sexual incompetence or wilful refusal to consummate the marriage, but the judge was not satisfied that the marriage had not been consummated. She accordingly petitioned for divorce on the ground of cruelty through a failure of the husband, consistent only with determination, properly to give her those sexual rights to which she was entitled, with the result that her health deteriorated and at one time at least was in a serious condition.

Mr. Justice Wallington did not doubt that the conduct of the husband, if continued, would have produced a serious and dangerous deterioration in her health, nor that he must have understood the wrong and injury that he was doing to his wife. The judge did not suppose that her whole well-being depended on sexual intercourse or that she thought that it did. Some women, he said, may be so constituted that their health is not affected by repeated partial intercourse, such as coitus interruptus, while other women enter into the marriage state hoping to fulfil one of its most important functions—the bearing of children. When such women are denied the normal means of child-bearing and their sexual functions are abused by frequent coitus interruptus, especially when it follows substantial periods of complete denial of intercourse, their health is likely to be affected. In his opinion the case before him fell into this class, and he granted the wife her decree. He mentioned, however, during his judgment that mere abstention by the husband from intercourse could not amount to cruelty or give the wife any remedy, even though it might injure her health.

There must, it appears, be aggravating circumstances of the kind related here, such as long periods of total abstention and callous indifference to the harm that was being done. Where such circumstances are present, however, a spouse may have a remedy if the nullity remedy fails.

[1] *Walsham* v. *Walsham*, 1949, 1 All E.R. 775.

Universities and Colleges

UNIVERSITY OF OXFORD

In a Congregation held on July 16 the following degrees were conferred:

D.M.—J. P. Childs.

B.M.—D. A. T. Tizard, R. T. T. Warwick, W. J. C. Symonds, R. W. Barr Brown, R. Kelly-Wiseham, Sheila J. Thorogood, Anne M. M. Oriel, *G. A. Rose, *D. G. R. Campbell, *G. de B. Mitford-Barberton, *J. W. Yeandle-Hignell, *Susan E. Scott-Stokes.

In a Congregation held on July 30 the following degrees were conferred:

D.M.—G. P. Maher-Loughnan.

M.Ch.—G. J. Fraenkel.

B.M.—G. F. Harris, J. C. F. Poole, R. O. Payne, Patricia M. Gilham, Sabine J. Strich, Alison D. Reid, *D. J. Woolford, *T. C. Barns, *Ruth E. Trilling.

*In absence.

UNIVERSITY OF CAMBRIDGE

Kendal Cartwright Dixon, Ph.D., M.B., B.Chir., has been appointed University Lecturer in Chemical Pathology for three years from October 1.

Mary Etheldreda Priscilla Hele, M.B., B.Chir., has been appointed to the Benn W. Levy Research Studentship in Biochemistry for the period October 1, 1949, to September 30, 1950.

In Congregation on July 30 Kenneth Frank Wilsdon, B.M., B.Ch., F.R.C.S.Ed., was admitted to the degree of M.A. by incorporation.

The following medical degrees were conferred in Congregation on July 30:

M.D.—*A. P. Bentall, *A. Leese, *J. R. Squire, *T. P. Pattinson, *A. P. Norman, J. M. Lipscomb, R. Fletcher.

M.B., B.CHIR.—*R. N. Twistington Higgins, *J. L. Whitby, *G. K. Barker, *P. J. Crosland-Taylor, *M. A. Epstein, *H. P. Lambert, *D. W. L. Leslie, *P. T. Perkins, *A. Polak, *M. T. Pym, *C. B. Walker, *J. F. Watkins, *E. C. B. Hall-Craggs, *L. B. Hunt, *R. G. Watkinson, R. W. Fairhead, *D. Bulmer, *E. H. R. Ford, *D. G. A. Leggett, *J. D. Marsh, *B. W. Peckett, *J. H. Rack, *T. J. Sullivan, I. R. McWhinney, *D. Gough, I. P. James, *P. E. Bodkin, *G. A. Court, *G. A. Gresham, *J. B. Self, *P. W. Thompson, *I. S. Waller, *M. Wilkinson, D. A. A. Beardsmore, E. A. Cooper, E. J. Watson-Williams, *E. C. A. Bott, *J. F. Boyle, *C. McCance, *T. C. K. Marr, *J. H. Neame, *C. A. Rogerson, *T. E. Stockley, *S. A. Wartski, *C. C. Clapham, *J. F. Soothill, *J. Stevens, P. A. Freeman, *D. S. Kerr, M. K. Sykes, *A. J. Lane, *W. P. L. Morrison, *J. M. Roberts, *L. R. Spencer, *R. A. Struthers, *D. G. Thompson, *H. B. Ll. Williams, L. C. Hurst, E. W. P. Jones, *A. Bates, *J. Armstrong, *B. F. Whitehead, R. D. Eagland, M. J. Kehoe, *Janet F. C. Callow, *Ellen Veldhuyzen, *Dorothea P. Wagstaff, *Dinah D. Webb, Billie I. Brown, Patricia B. Corston, Brenda M. Grimmett, *B. J. Hockey, H. R. Odlum.

*By proxy.

In Congregation on August 20 the honorary degree of D.Sc. was conferred on the following: Viscount Addison, K.G., M.D., F.R.C.S., Lord Privy Seal, Leader of the House of Lords, and Chairman of the Medical Research Council; Carl Ferdinand Cori, Professor of Biochemistry in the University of Washington School of Medicine; Sir Charles Robert Harington, Ph.D., F.R.S., Director of the National Institute for Medical Research; Kaj Linderström-Lang, Director of the Carlsberg Laboratory, Copenhagen; Arne Wilhelm Kaurin Tiselius, Professor of Biochemistry in the Royal University of Uppsala, Sweden; Jacques Tréfouël, Membre de l'Institut et de l'Académie Nationale de Médecine and Directeur de l'Institut Pasteur, Paris.

UNIVERSITY OF GLASGOW

The following candidates have been approved at the examination indicated:

D.P.H.—Muriel S. Alexander, J. R. H. Berrie, G. S. Carrick, Flora C. Cowan, N. R. Cowan, Agnes C. Davidson, Katharin I. Kerr, Ruth A. Keymer, D. Livingstone, Margaret J. Macarthur, D. MacInnes, Ann K. MacLennan, J. Maxton, Agnes W. O'Gorman, Martha G. Robson (née Kennedy), Betsy D. Scott, M. Silver, J. M. Wallace, Elizabeth M. Whiteside, Jessie E. Wilson, T. S. Wilson.

UNIVERSITY OF LONDON

Anthony Clegg Cunliffe, M.D., has been appointed to the University Readership in Bacteriology tenable at King's College Hospital Medical School, from October 1.

John Laurence Malcolm, M.B., Ch.B., has been appointed to the University Readership in Experimental Physiology tenable at St. Mary's Hospital Medical School, from October 1.

INFECTIOUS DISEASES AND VITAL STATISTICS

We print below a summary of Infectious Diseases and Vital Statistics in the British Isles during the week ended August 20. [No. 33

Figures of Principal Notifiable Diseases for the week and those for the corresponding week last year, for: (a) England and Wales (London included). (b) London (administrative county). (c) Scotland. (d) Eire. (e) Northern Ireland.

Figures of Births and Deaths, and of Deaths recorded under each infectious disease, are for: (a) The 126 great towns in England and Wales (including London). (b) London (administrative county). (c) The 16 principal towns in Scotland. (d) The 13 principal towns in Eire. (e) The 10 principal towns in Northern Ireland.

A dash — denotes no cases; a blank space denotes disease not notifiable or no return available.

Disease	1949					1948 (Corresponding Week)				
	(a)	(b)	(c)	(d)	(e)	(a)	(b)	(c)	(d)	(e)
Cerebrospinal fever	22	2	7	3	1	26	4	18	—	—
Deaths		—	—				—	—		
Diphtheria	59	8	23	1	6	116	14	23	14	5
Deaths	2	—	—	—	1	—	—	—	—	—
Dysentery	35	4	83	—	1	111	10	58	3	—
Deaths				—	—				—	—
Encephalitis lethargica, acute	3	—	1	—	—	3	—	—	—	—
Deaths		—					—			
Erysipelas			16	6	1			30	5	3
Deaths		—					—			
Infective enteritis or diarrhoea under 2 years				62					45	
Deaths	19	—	4	6	6	32	3	21	2	—
Measles*	2,120	158	57	96	37	4,611	189	43	39	25
Deaths†			—	—	—			—	—	
Ophthalmia neonatorum	47	1	17	—	—	59	3	17	—	—
Deaths										
Paratyphoid fever	30	1	3 (B)	8 (B)	—	20	3	1 (B)	—	—
Deaths	—	—	—	—	—	—	—	—	—	—
Pneumonia, influenzal	245	13	2	2	6	266	9	—	3	1
Deaths (from influenza)‡	6	—	—	—	—	4	—	—	—	—
Pneumonia, primary			127	20				98	12	
Deaths	103	11		4	8	112	12		2	4
Polio-encephalitis, acute	22	4				6	—			
Deaths										
Poliomyelitis, acute	273	31	14	1	2	72	10	3	4	2
Deaths§	14	2				1	—			
Puerperal fever		—	5				—	8		—
Deaths										
Puerperal pyrexia‖	80	6	5	—	1	106	9	8	—	—
Deaths		—						—		
Relapsing fever	—	—			—	—	—			—
Deaths										
Scarlet fever	678	47	136	61	43	736	38	134	74	22
Deaths†			—	—	—			—	—	—
Smallpox	—	—	—	—	—	—	—	—	—	—
Deaths				—	—				—	—
Typhoid fever	6	3	1	2	1	8	—	1	2	2
Deaths	1	—	—	—	—	—	—	—	—	—
Typhus fever	—	—	—	—	—	—	—	—	—	—
Deaths				—	—				—	—
Whooping-cough*	1,637	82	41	118	82	3,260	315	24	114	17
Deaths	4	1	1	1	—	13	1	1	—	—
Deaths (0–1 year)	220	29	27	14	19	230	28	52	6	7
Infant mortality rate (per 1,000 live births)										
Deaths (excluding still-births)	3,910	635	513	167	108	3,771	583	547	125	92
Annual death rate (per 1,000 persons living)			10·3	10·3				11·0		
Live births	7,087	1099	831	400	247	7,568	1281	917	353	241
Annual rate per 1,000 persons living			16·7	24·8				18·5		
Stillbirths	188	29	21			211	25	28		
Rate per 1,000 total births (including stillborn)			25					30		

* Measles and whooping-cough are not notifiable in Scotland, and the returns are therefore an approximation only.

† Deaths from measles and scarlet fever for England and Wales, London (administrative county), will no longer be published.

‡ Includes primary form for England and Wales, London (administrative county), and Northern Ireland.

§ The number of deaths from poliomyelitis and polio-encephalitis for England and Wales, London (administrative county), are combined.

‖ Includes puerperal fever for England and Wales and Eire.

EPIDEMIOLOGICAL NOTES

Q Fever in London

On July 11, 12, and 13 three members of the staff of the pathological department and one nurse at a London hospital became ill with what appeared to be atypical pneumonia. All recovered, but subsequent investigation has shown that all now have significantly high agglutinations against *Rickettsia burneti*. The rickettsia has also been recovered from one sample of blood. The usual incubation period (10–24 days) has now expired, and there is no evidence of further spread of the disease in the hospital. The source of infection is being investigated.

This is believed to be the first occasion on which *R. burneti* has been recovered in this country. Although Stoker has found suggestively high titres in a few individuals, there has heretofore been no unequivocal evidence of a source of infection here.

Q fever was first distinguished as a human disease in Queensland, Australia, in 1935, and was thought to be tick-borne. Later, in Chicago and Texas, outbreaks occurred in slaughterhouses and were attributed to the inhalation of tick faeces or some other rickettsial-contaminated material. During 1944–5 the disease was recognized in Greece and the North Apennines. It has also been reported from Switzerland, France, Germany, Turkey, Morocco, and Algeria. In the U.S.A. endemic foci have been identified in California. In some outbreaks ticks have not been involved, and the mechanism of spread remains uncertain.

Although the present episode may be no more than an isolated importation it calls for special vigilance. Early recognition of the disease and the correction of any environmental factor likely to facilitate spread may prevent the establishment of endemicity. It is therefore desirable that outbreaks of atypical pneumonia should be brought to the notice of medical officers of health, especially infection in persons handling meat and milk in slaughterhouses and dairies. Facilities for routine laboratory diagnosis are not available in hospital laboratories. Serological studies will be undertaken through the Virus Reference Laboratory at Colindale in selected instances. Not all strains of Q fever are antigenically identical.

Q fever is an acute febrile disease closely simulating virus pneumonia. It is not easily differentiated from influenza, primary atypical pneumonia, psittacosis, and other obscure fevers. The disease is characterized by sudden onset which can be dated, headaches (commonly frontal, behind the eyes), weakness, sweating and chills, and body aches. Pleuritic pain and cough often occur, and the sputum may be blood-stained, although expectoration is as a rule scanty. As in virus pneumonia, physical signs are relatively slight compared with the radiological findings, which are, generally speaking, indistinguishable from those of primary atypical pneumonia. The white count is normal or decreased, with a relative lymphocytosis. Fever is usually high and persists for from one to ten days or more; in most cases it is of from three to six days' duration. Anorexia may be pronounced at the onset, and the fever may be very debilitating.

Q fever is distinguished from the other rickettsial diseases (epidemic typhus, scrub typhus, Rocky Mountain spotted fever, rickettsialpox) by the rarity of cutaneous lesions. A fine vesicular eruption of short duration may occur in less than 10% of cases. In Q fever the Weil–Felix reaction is negative. (See also an annotation in our issue of June 12, 1948, p. 1145.)

Poliomyelitis

Notifications in England and Wales in the week ended August 27 were poliomyelitis 258 (273), polio-encephalitis 22 (22). Figures for the previous week are shown in parentheses.

The following counties reported multiple cases (poliomyelitis and polio-encephalitis together): London 34 (35), Berkshire 3 (11), Cheshire 8 (6), Cornwall 5 (8), Derby 2 (9), Devon 4 (9), Dorset 2 (1), Durham 3 (2), Essex 13 (10), Gloucester 15 (5), Hertford 6 (3), Kent 9 (6), Lancaster 33 (29), Lincolnshire, Lindsey 3 (3), Middlesex 17 (13), Northampton 4 (6), Northumberland 6 (7), Nottingham 7 (10), Somerset 7 (5), Southampton 16 (11), Stafford 4 (6), Suffolk East 2 (0), Suffolk West 2 (3), Surrey 5 (7), Sussex East 4 (2), Sussex West 2 (3), Warwick 7 (4), Wiltshire 3 (4), Yorkshire East Riding 3 (1), Yorkshire North Riding 4 (1), Yorkshire West Riding 33 (50), Monmouth 2 (2).

Of the 15 cases reported from Gloucestershire 14 were in Bristol C.B. For the first time in five weeks there has been a small fall in notifications. Thus the curve of incidence so far this year has been very similar to that in 1947 though at a much lower level. The figures of notifications for the corresponding week (Week 34) of 1947 were: poliomyelitis 626, polio-encephalitis 50.

Discussion of Table

In *England and Wales* infectious diseases were less prevalent during the week. There were decreases in the notifications of measles 1,106, whooping-cough 101, dysentery 27, and diphtheria 19. There was an increase of 37 in the notifications of acute poliomyelitis.

The largest falls in the notifications of measles were Durham 104, Lancashire 85, Kent 80, Northumberland 71, Norfolk 69, Glamorganshire 68, London 65, and Warwickshire 62. The largest variations in the returns for whooping-cough were decreases in Yorkshire West Riding 38 and Staffordshire 33, with an increase of 40 in Lancashire.

Notifications of diphtheria reached a new record low level and were 14 below the previous lowest return. The chief feature of the returns for diphtheria during the week was a decrease in notifications in London 6.

Of the 30 cases of paratyphoid fever 20 were notified in Lancashire (Liverpool C.B. 8). The largest return for dysentery was 10 in Lancashire (Liverpool C.B. 6). An outbreak of food poisoning occurred in Carmarthenshire, and 196 cases were notified in the urban and rural districts of Llanelly.

In *Scotland* there were increases in the notifications of dysentery 29 and scarlet fever 26. Of the 83 cases of dysentery 62 were notified in the city of Glasgow. In the western area there were 9 more notifications of diphtheria than in the preceding week. The rise in the incidence of scarlet fever was contributed by the western area.

In *Eire* increases were recorded in the notifications of whooping-cough 43 and measles 23. There was a decrease of 23 in the notifications of diarrhoea and enteritis. Outbreaks of whooping-cough were notified from Donegal, Donegal R.D. 27, and Dublin, Balrothery R.D. 14, and there was an outbreak of measles in Carlow, Carlow R.D. 18.

In *Northern Ireland* an increase of 14 in the notifications of whooping-cough was the only noteworthy change in the trends of infectious diseases.

Week Ending August 27

Notifications of infectious diseases in England and Wales during the week included: scarlet fever 718, whooping-cough 1,671, diphtheria 52, measles 1,778, acute pneumonia 222, cerebrospinal fever 18, acute poliomyelitis 258, acute polio-encephalitis 22, dysentery 90, paratyphoid fever 25, typhoid fever 10, food poisoning 171.

Medical News

Films on Haematology

The first two of a series of films on "Animated Haematology" were recently shown to an audience in London. The films were produced by the Armour Laboratories in Chicago, with the collaboration of the Department of Medicine of the University of Illinois. The first is entitled "The Haemopoietic Principle," and the second "Bone Marrow." They are 1,600-foot, 16-mm. silent colour films and are suitable for teaching purposes and for showing at medical meetings. They may be borrowed free of charge from Armour Laboratories Limited, 2, Lindsey Street, London, E.C.1.

Pharmaceutical Research Fellowships

The Pharmaceutical Society announces the award of two Fellowships of the value of £300 a year for two years. The Ransom Fellowship has been won by Mr. R. A. Webb, B.Pharm., B.Sc., who will do research work in organic chemistry at the University of London School of Pharmacy. Mr. B. K. Martin, B.Pharm., won the society's own scholarship and will undertake an investigation of the synthesis of pteridines and other related heterocyclic compounds at Nottingham University.

Wills

Dr. John Christopher Davies, of Shrewsbury, left £41,960. Mr. Arthur Hedley Clarence Visick, of Fulford, Yorks, left £13,589. Dr. Henry Colin Maclaren, of Carlisle, left £5,970. Dr. David Cyril Thomas, of Winterton, Norfolk, left £13,130. Dr. Frederick Barnes Elwood, of Belfast, left £33,524. Mr. Ernest Lewis Lilley, of Scraptoft, Leics, left £44,038, including £250 to the Charities Fund of the B.M.A.

COMING EVENTS

N.A.P.T. and Medical Officers of Health

A joint meeting of the National Association for the Prevention of Tuberculosis and the Society of Medical Officers of Health will take place in B.M.A. House on Thursday, September 15, at 2.30 p.m. The chairman will be Professor R. H. Parry, president of the Society of Medical Officers of Health and medical officer of health, City and County of Bristol. The object of the meeting is to exchange views and experience on social and aftercare arrangements by local health authorities under the National Health Service. The following speakers will lead the discussion: Sir Allen Daley, London County Council; Dr. G. W. H. Townsend, Buckinghamshire County Council; Dr. W. Alcock, Burton-upon-Trent; Dr. Neville Irvine (B.C.G. Vaccination); and Miss Anne Topley, Care Almoner, Surrey County Council.

Cerebral Palsy

Dr. Earl R. Carlson, medical director of the School of Corrective Motor Education, Long Island, New York, will address a meeting to be held under the auspices of the British Council for the Welfare of Spastics at the Royal Society of Medicine (West Hall), 1, Wimpole Street, London, W., on Wednesday, September 21, at 5 p.m. The American film, "A Day in the Life of a Cerebral Palsied Child," will be shown after the address.

King's College Hospital Medical School

Sir Hugh Cairns will deliver the inaugural address at the opening of the 1949–50 session of King's College Hospital Medical School on Friday, September 30, at 3 p.m., with Sir William Gilliatt in the chair.

No. 2 General Hospital

The third reunion dinner of No. 2 General Hospital will be held at Simpson's Restaurant, 100, Strand, London, W.C., on Saturday, October 8, at 6.30 for 7.15 p.m., with Colonel E. Scott in the chair. Tickets (14s. for officers and nursing officers; 12s. 6d. for other ranks) may be obtained from Mr. A. E. Porritt, C.B.E., F.R.C.S., 10, Upper Wimpole Street, London, W.1.

French Refresher Course

A refresher course in medicine and surgery—Les Entretiens de Bichat—will be held at the Bichat Hospital, Paris, on October 10–15. Further particulars may be obtained from L'Expansion Scientifique Française, 23, Rue du Cherche-Midi, Paris, 6e.

American Public Health Association

The 77th Annual Meeting of the American Public Health Association and meetings of related organizations will be held at the Hotels Statler and New Yorker, New York City, on October 24–28. Information may be obtained from Dr. Reginald M. Atwater, Executive Secretary, American Public Health Association, 1790, Broadway, New York City.

Alvarenga Prize and Lecture

On July 14 the College of Physicians of Philadelphia (19, South Twenty-second Street, Philadelphia, 3, U.S.A.) awarded the Alvarenga Prize for 1949 to Owen Harding Wangensteen, M.D., Ph.D., Professor of Surgery, University of Minnesota, for his important contributions to the aetiology and therapy of gastric and duodenal ulcer. Dr. Wangensteen will deliver the Alvarenga Lecture on this subject at the College of Physicians of Philadelphia on November 2. The Alvarenga Prize was established by the will of Pedro Francisco daCosta Alvarenga, of Lisbon, Portugal, an Associate Fellow of the College of Physicians, of Philadelphia, to be awarded annually by the College on the anniversary of the death of the testator, which took place on July 14, 1883.

SOCIETIES AND LECTURES

Tuesday

EDINBURGH POSTGRADUATE BOARD FOR MEDICINE.—At Anatomy Lecture Theatre, Edinburgh University, September 13, 4.30 p.m., "*The Metabolic Response to Injury*," by Dr. D. P. Cuthbertson.

Wednesday

INSTITUTE OF PSYCHIATRY (UNIVERSITY OF LONDON).—At Maudsley Hospital, Denmark Hill, London, S.E., September 14, 5 p.m., "*Neurological Organization for Motion*." Public Lecture by Professor Warren S. McCulloch (University of Illinois, Chicago). All interested are invited.

Thursday

INSTITUTE OF PSYCHIATRY (UNIVERSITY OF LONDON).—At Maudsley Hospital, Denmark Hill, London, S.E., September 15, 2.15 p.m., "*Emotion from the Physiological Viewpoint*," Public Lecture by Professor E. Gellhorn (University of Minnesota). All interested are invited.

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE, 28, Portland Place, London, W.—September 15, 3 p.m., "*World Trends in the Teaching of Social Medicine and Public Health*," Bengué Memorial Award Lecture by Professor René Sand (University of Brussels).

APPOINTMENTS

Dr. D. J. M. Mackenzie, O.B.E., Director of Medical Services, Nyasaland Protectorate, has been appointed an Official Member of the Legislative Council of the Protectorate.

EAST ANGLIAN REGIONAL HOSPITAL BOARD.—*Consultant Psychiatrist, Fulbourn Mental Hospital*, R. L. Buttle, M.R.C.S., L.R.C.P., D.P.M. *Second Consultant Pathologist, Norfolk and Norwich Hospital*, A. L. M. Christie, M.Sc., Ph.D., M.B., B.S. *Consultant Chest Physician, Ipswich and East Suffolk Area*, C. J. Stewart, M.D., D.Obst.R.C.O.G.

RAFTERY, LILIAN, M.R.C.S., L.R.C.P., M.M.S.A., M.R.C.O.G., Honorary Visiting Gynaecologist, King George V Springfield Hospital for Tuberculosis, Durban, South Africa.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Eedy.—On August 22, 1949, at Mansfield Nursing Home, to Françoise (née Chanu), wife of Dr. B. N. Eedy, a daughter—Bernardine.

Heap.—On August 21, 1949, at "One Oak," Pickering, Yorks, to Berry, wife of Dr. K. I. Heap, a son.

DEATHS

Alderson.—On September 3, 1949, Wilfred Ernest Alderson, M.D., formerly of 56, Highbury, Newcastle-upon-Tyne, aged 76.

Berry.—On August 31, 1949, at 3, All Saints Road, Clifton, Bristol, Beatrice Catharine, the wife of Professor R. J. A. Berry, M.D., F.R.S.E., aged 71.

Critchley.—On August 31, 1949, Samuel Edward Critchley, M.B., Ch.B., of 532, Chorley Old Road, Bolton.

Dewar.—On September 1, 1949, at Heathfield House, Whitefield, near Manchester, James Dewar, M.B., B.Ch., of Bury.

Fuller.—On August 31, 1949, at 5, Regent's Court, Hanover Gate, London, N.W., Charles Arthur Fuller, V.R.D., M.B., late of Cawnpore, India, aged 80.

Fulton.—On August 30, 1949, at 57, Burnley Lane, Chadderton, Frederick Fulton, L.R.C.P.&S.Ed., L.R.F.P.S.Glas.

Hernaman-Johnson.—On September 3, 1949, at Rotherfield Road, Carshalton, Francis Hernaman-Johnson, M.D., F.F.R., aged 70.

Hincks.—On August 26, 1949, at Wells, Somerset, Arthur Cecil Hincks, *M.C.*, M.B., Ch.B.

Lindow.—On August 26, 1949, Eric Delafield Lindow, M.R.C.S., L.R.C.P., of 19, Beaufort Gardens, London, S.W., late Malayan Medical Service.

Morgan.—On September 1, 1949, at North Walsham, Norfolk, Edward Morgan, M.R.C.S., L.R.C.P., aged 69.

Peacey.—In April, 1949, Winifred Peacey, M.R.C.S. L.R.C.P., of Hayle, Cornwall.

Stewart.—On September 3, 1949, at Wilton Villa, Ashton Road, Denton, Manchester, William Stewart, M.D., M.Ch.

Wells.—On September 2, 1949, at Wilcott, Sanderstead, Surrey, Harry Vernon Wells, F.R.C.S., aged 49.

Any Questions ?

Osteochondritis Dissecans

Q.—*What are the aetiology, prognosis, and treatment of osteochondritis dissecans?*

A.—The cause of osteochondritis dissecans is not known with certainty. It is generally agreed that it results from local loss of blood supply to an area of bone, but the primary cause of this is debatable. It is often attributed to trauma, which may lead to thrombosis of an end artery supplying a segment of bone. This is a reasonable hypothesis, and it is supported by the observation that in the knee the area of osteochondritis usually lies on the infero-lateral aspect of the medial femoral condyle immediately opposite a prominent tibial spine; it is supposed that impingement of the condyle against the tibial spine is the primary factor. When osteochondritis occurs in other areas of the knee, or in other joints, there is often—though by no means always—a history of previous direct injury. The pathological course of osteochondritis dissecans in the knee may be summarized as follows. Initially there is an area of avascularity of bone, which is shown in the radiographs as an area of increased density. The overlying articular cartilage degenerates. After a variable period, usually many months, the avascular fragment of bone separates and forms a loose body, leaving a crater in the bone which becomes filled with fibrin and later with fibrocartilage.

When the diagnosis is made before the fragment has separated it is often wise to await spontaneous separation, heavy use of the joint being avoided in the meantime. But if the knee is opened the avascular fragment should be gouged out, leaving a clean vascular bed. In doing this it is sometimes difficult to define the line of demarcation between avascular and healthy bone. When operation is deferred until spontaneous separation has occurred all that is necessary is to remove the loose body or bodies. After operation, a few weeks' rest, with intensive quadriceps exercises, is advisable. The prognosis depends on the size of the avascular fragment and of the resulting cavity in the articular surface, and on the position of the lesion. When the cavity is small and situated away from the major weight-bearing area of the condyle—for example, at the lateral aspect of the lateral femoral condyle—the prognosis is good; but when the main weight-bearing surface of a joint is involved, and particularly if the lesion is large, there is a risk of the development of degenerative arthritis months or years later owing to the loss of normal articular cartilage over the area of the lesion.

Treatment of Burns

Q.—*What is the modern treatment of burns?*

A.—Experience during and since the war has shown that treatment should have these aims: (1) to relieve the pain which follows the accident, and avoid pain later; (2) to prevent the onset of "shock," and steer the patient through it if it develops, by carefully controlled fluid replacement; (3) to prevent and control infection throughout the period of recovery; (4) to ensure regeneration or replacement of skin as early as possible; (5) to avoid or diminish metabolic disturbances resulting from injury, fever, or anaemia; (6) to encourage normal functioning of the injured parts and of affected joints, etc., and to maintain the patient's morale throughout; (7) by secondary repair or "plastic" operations to correct any defect or deformity which remains or develops after healing is complete.

Amplifying these aims very briefly, the following recommendations are made: (1) For limb burns, if immediate pain is not severe, hold them under the cold tap; if pain is severe, give "omnopon" and scopolamine. Cover burn with a sterile (or freshly laundered) towel until dressing can be undertaken. The avoidance of later pain is almost entirely a question of preventing and controlling infection (see 3 below) and depends on patience and skill in carrying out the dressings. (2) For severe burns involving a large area, intravenous transfusion of plasma or serum should be started if possible within an hour of the

accident, or as soon thereafter as may be. The rate of flow and quantity of fluid to be given should be regulated by repeated haematocrit or haemoglobin estimations, and by the general condition of the patient (see Gibson and Brown, M.R.C. Memorandum No. 249, 1944). Transfusion can usually be discontinued after 24 to 30 hours. Plenty of fluid, but only by repeated sips, should also be given by mouth during the first few hours—sodium lactate 1.75% solution for choice. (3) Burned areas should be first cleaned carefully with "cetavlon" solution 1%. (An anaesthetic is very seldom required if omnopon and scopolamine have been given.) Penicillin cream, 400 units per gramme in a paste of lanette wax and water, is smeared on thickly, and plenty of dressing applied with firm pressure by crêpe bandages (these are essential). Burns of hand and forearm should be elevated above the level of the heart for the first three to five days to reduce effusion. (4) The first dressing should be left untouched (if comfortable and the initial fever has subsided) for from seven to 14 days. Subsequent dressings, if there is no manifest infection, should be applied at intervals of five to seven days. To burns infected with haemolytic streptococci penicillin cream should be applied at intervals of two days until the micro-organisms have disappeared. Whenever possible all dressings should be carried out in "clean" air—that is, in a room supplied with an abundant stream of filtered air—or, where this is not available, in a room with good window ventilation. Great care should be taken that perfect coverage of the burned areas is obtained and maintained. For superficial burns, avoid infection, and epithelial regeneration will need no encouragement. For burns involving "whole-skin" loss of limited extent, grafting may often be undertaken with great advantage on the day of the accident (or within three days), after the burned tissues have been excised. Grafting at later periods should not usually be undertaken when haemolytic streptococci are present. Flexures in particular should be grafted very early. (5) Patients with severe burns should be given an abundant high-protein, well-balanced diet after the first two or three days, with in addition a liberal allowance of ascorbic acid. Anaemia, if severe, may call for one or more blood transfusions. (6) Early physiotherapy and occupational therapy are of value; great gentleness and patience in applying dressings are essential throughout the whole course of treatment.

Incubation Period of Tuberculosis

Q.—*Is any information available about the length of the latent period between infection with the tubercle bacillus and clinical manifestations of the disease?*

A.—In most cases infection with the tubercle bacillus is not followed by clinical manifestations in the sense of recognizable symptoms. A positive tuberculin reaction is the only evidence that infection has occurred. Wallgren has made a special study of "the time-table of tuberculosis" (*Tubercle*, 1948, 29, 245). He found that the important initial manifestations of tuberculous infection in children included transient fever, raised erythrocyte sedimentation rate, erythema nodosum, and the development of tuberculin-sensitivity and of the primary complex. The exact time infection occurred is often difficult to determine, but his studies suggest that the incubation period is usually about five to six weeks, although in exceptional cases it may be as short as three or as long as eight weeks.

Testing Swimming-bath Water

Q.—*A recent article seems to suggest that the results obtained when testing swimming-bath water for residual chlorine with o-tolidine reagent may not be reliable enough, and that, even if the water shows a high chlorine reading, this chlorine is not necessarily all available for sterilization purposes. Is this correct? The bacteriological examination of water means a wait of three to four days. If the residual chlorine test can still be regarded as reliable, it has obvious advantages.*

A.—Monochloramine, dichloramine, and even nitrogen trichloride may be produced when chlorine is added to water containing ammonium, depending on the conditions. The *o*-tolidine reagent will react with all of these. It does not, in the ordinary test, differentiate clearly between these, and it is therefore true to say that the test does not give a determination of chlorine alone. Nevertheless, as the chloramines are also bactericidal, although slower in action than chlorine, the *o*-tolidine reagent is probably still the best to employ for the control of purity. It is, of course, necessary in the control of swimming-bath water to ensure that the test is used after the break-point has been passed. Much work has been done on modifications of the *o*-tolidine test, and it is probable that a method will soon be published which will determine the actual amounts of chlorine, chloramines, and nitrogen trichloride present in chlorinated water.

Hunner's Ulcer of Bladder

Q.—*What are the modern views on the treatment of Hunner's ulcer of the bladder? The condition is complicated by severe rheumatoid arthritis which contraindicates extensive operative procedures.*

A.—It is perhaps unnecessary to say that Hunner's ulcer of the bladder is one of the more intractable conditions with which the genito-urinary specialist has to deal. Many forms of treatment have been tried, but without avail. One recognized form of treatment is distension of the bladder. The patient is taken into hospital or nursing-home and the bladder distended with increasing amounts of fluid. A solution of silver nitrate is often used for this purpose, beginning with a strength of 1 in 8,000 and gradually increasing up to 1 in 1,000. The bladder is distended once daily, the distension and strength of solution being increased according to the toleration of the patient. However, the writer has had little success with this treatment and it has the disadvantage of being painful; the only cure he has obtained when the condition is well established has been by operative measures. The whole of the affected area was excised, and the result was complete cure. If the patient is in great distress, so that life has become a misery, it would be justifiable to operate.

Fröhlich's Syndrome

Q.—*When examining school-children between the ages of 10 and 14 years one occasionally comes across a very fat child—if male, with one or both testes undescended, or, if female, with delayed menstruation. This combination suggests some endocrine dysfunction. It would be interesting to learn if any of the endocrine glands are involved, and if any hormone treatment is available. The hormone therapy for undescended testicle does not reduce the obesity, neither does dietetic treatment. What investigations are needed in these cases and what treatment?*

A.—Adiposity with failure of sexual development and failure of growth is known as Fröhlich's syndrome, and in some classifications a failure of growth is not regarded as essential for the diagnosis. However, from the point of view of treatment, the obesity falls into the same category as idiopathic obesity, for which there is no direct hormone therapy, and for which, as has been frequently indicated in these columns (Aug. 21, 1948, p. 408; Oct. 30, 1948, p. 808; March 5, 1949, p. 421; July 16, 1949, p. 189), the conventional treatment is diet, diuretics, and appetite-reducers, such as amphetamine sulphate. *X*-ray examination of the pituitary fossa should be carried out, but is usually negative.

Price's Precipitation Reaction

Q.—*How does Price's precipitation test for syphilis compare with other precipitation tests and the Wassermann reaction as regards specificity and sensitiveness? What is the technique of this reaction?*

A.—According to its originator, Price's precipitation reaction is less sensitive than the Kahn test, but considerably more specific. It is less sensitive than the Wassermann reaction, but of about the same degree of specificity. The technique of the test is described by Price, I. N. Orpwood (*J. clin Path.*, 1948, **1**, 91), and his experience in the use of the test is given in *Brit. J. vener. Dis.* (1949, **25**, 67).

Esbach's Test

Q.—*Esbach's test can be very misleading, and it is surprising that textbooks do not mention this. The only reference I have found is on page 640 of Martindale's Extra Pharmacopoeia, 1943 ed., vol. 2. By employing a simple method I have been able to arrive at a more correct quantitative reading of albumin content, and would be glad of an opinion about the correctness of the method and the accuracy of the deductions. Finding a heavy precipitate in Esbach's albuminimeter which I could not reconcile with clinical findings, I turned out the column of fluid and precipitate into a test-tube and boiled it for a few minutes, when much of the precipitate went into solution. After cooling, the contents were transferred into Esbach's tube and allowed to stand for another 24 hours, at the end of which the reading, which had originally been 4 g. per litre, was only 0.5 g. As boiling brings down albumin, it must be concluded that the original high reading was accounted for by substances other than albumin. What are the other substances which precipitate in Esbach's reagent?*

A.—On account of its simplicity, Esbach's test is often used by clinicians, but it gives only a rough measure of protein content and is too inaccurate for use in the laboratory. In this test it is assumed that a given weight of protein precipitated from urine always occupies the same volume regardless of variations in the composition and density of the urine. This cannot be true, because the state of aggregation of colloidal precipitates of proteins is known to vary with physical conditions. Furthermore, the test has not been properly standardized. For instance, there are variations in the composition of the recommended precipitating solution, and the temperature conditions are not specified. The method given in Martindale's *Extra Pharmacopoeia*, which involves heating to 180° F. (82.2° C.) and centrifuging for a few minutes, might well yield different results from the more usual routine. Substances other than protein which may be precipitated are uric acid and urates, and the excretion product of "uroselectan"; other substances mentioned as interfering with the result are creatinine, resin, unspecified acids, methylene blue, and alkaloids.

To explain the decrease after boiling reported in the question would require a careful chemical examination of the particular specimen tested, but it is possible that the boiling may have converted some protein to metaprotein, or have changed it physically so that it occupied less volume. Alternatively, as the question suggests, boiling may have removed some interfering substance. The inquirer's variation of the test—namely, boiling the mixture—has probably little to recommend it. If a satisfactory determination of protein is required, then a recognized chemical estimation should be used—for example, a Kjeldahl or biuret determination. It is unfortunate that several textbooks describe Esbach's test without giving any warning of its inaccuracy, but Harrison makes some pertinent comments on the test (*Chemical Methods in Clinical Medicine*, 3rd ed., 1947, Churchill, pp. 44 and 52).

Sex Hormones and the Hair

Q.—*Three women in their middle fifties have complained recently of a lack of lustre in their hair. In each case the patient dated the condition from a large intake of stilboestrol. The hair was lifeless and in texture resembled cat's fur. Stilboestrol has been withdrawn. Would the male hormone in suitable doses help to restore the condition of the hair?*

A.—It is very unlikely that stilboestrol has adversely affected the scalp hair, as in Simmonds's disease it improves the texture and colour of the hair (S. L. Simpson, *Proc. R. Soc. Med.*, 1948, **41**, 192, and Section of Endocrinology, p. 6). It is theoretically possible that the dosage was so large as to produce degranulation of the anterior pituitary cells and a type of hypopituitarism. Testosterone, or methyl testosterone, improves the lustre and colour of the hair in Simmonds's disease (ibid.), and might therefore prove helpful in the cases referred to. In very large doses, however, it causes some loss of scalp hair in the temporo-frontal regions, as in virilism; it also makes the hair somewhat coarse in texture.

Delayed Speech

Q.—*What would cause backwardness in speech in a girl aged 4, who seems healthy and intelligent but is still unable to form any sentence of more than two or three words, which are unintelligible to a stranger? She has a brother aged 6 who has always spoken remarkably well for his age, and she meets other children frequently. Is there any treatment?*

A.—There are many causes of retardation of speech in normal children, and some very intelligent children have been known to delay talking until after 4 or 5 years of age and then to speak fluently. It is possible that in this case a cause for the delayed speech may be the unusual ability of the elder brother, who might unwittingly deter his younger sister from talking, either by acting as interpreter so that she need not voice her own demands or by demonstrating too high a standard in a way unintelligible to her. It can be very difficult for a younger child to understand an older one talking rapidly. And then much depends on the way parents and other adults speak: this should be clearly and slowly, encouraging response but without demanding it. There is, of course, a serious possibility of speech being delayed by some type of deafness, and this could be ascertained by tests such as those devised for young children by Dr. and Mrs. Ewing, of Manchester.

NOTES AND COMMENTS

Delirium Tremens.—Dr. R. M. YOUNG (Macclesfield) writes: I have been shocked to read both the answer about delirium tremens and the note from Dr. A. E. Carver ("Any Questions?" July 23, p. 242, and August 27, p. 496). Surely it has been accepted for many years that delirium tremens is a manifestation of vitamin-B_1 deficiency, due to the anorexia of the alcoholic in combination with failure of absorption due to the chronic poisoning of the alimentary canal. Be that as it may, your correspondents will find that delirium tremens responds in a matter of hours, almost minutes, to adequate vitamin-B therapy parenterally. A proprietary preparation containing suitable amounts of the whole group exists, or 200 mg. of nicotinic acid can be given intravenously. Aneurin hydrochloride (50 mg.) is given as well. The choice of sedative scarcely matters, but 2–3 oz. (56–84 ml.) of paraldehyde by mouth, suitably diluted, is excellent. A nasal tube may be used if the patient is not able to co-operate; and since, if this is so, exhaustion and dehydration are likely to be severe the opportunity should be taken to give a pint of milk or water with such added nourishment as is at hand—glucose, raw eggs, hydrolysed protein preparations. The patient will wake up clear, rational, and with a ravenous appetite which will complete the "cure." With any other form of treatment the death rate is high. In milder cases the vitamins seem to prevent the pangs of sudden withdrawal and the craving for a "hair of the dog" first thing in the morning. In these and in cases of delirium tremens after the crisis is past the vitamins can be given in tablet form in the following doses (t.d.s.): tab. acid. nicotin., 100 mg.; tab. aneurin hydrochlor., 10 mg.; tab. riboflavin, 3 mg. The patient should be warned to expect the hot flush which follows adequate dosage with nicotinic acid.

Correction.—Dr. ALAN J. HIRD (Glasgow) writes: I am sorry to say that an error has arisen in my article on Mikulicz's syndrome in the *Journal* of August 20. This is on p. 417, column 1, line 26. The term "deep x-ray therapy" (200 Kv) should apply only to the general or body irradiation. The local irradiation to salivary and lacrimal glands was with low-voltage therapy (85 Kv) so as to minimize the possibility of undesirable effects upon the eyes or secreting tissues.

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